

WEST Search History

DATE: Tuesday, October 15, 2002

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
side by side			result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR</i>			
L9	l5 near administ\$4	0	L9
L8	L7 not l5	0	L8
L7	gpipld	1	L7
L6	gpi adj pld	14	L6
L5	((antibod? near (IPG or inositophosphoglycan\$4)) or (GPI adj PLD))	22	L5
L4	((antibod? near (IPG or inositolphosphoglycan\$4)) or (GPI adj PLD))	22	L4
L3	L2 and GPI adj PLD	1	L3
L2	L1 and (IPG or (inositolphosphoglycan\$4))	33	L2
L1	(rademacher)[in] or (whitby)[in]	1303	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
L4 1 S L3 AND GPI-PLD
L5 1504 S (IPG OR (INOSITOLPHOSPHOGLYCAN?))
L6 4 S L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
L7 3 DUP REM L6 (1 DUPLICATE REMOVED)
L8 80 S L5 (10N) ANTIBOD?
L9 51 S L8 AND PD-19980327
L10 25 DUP REM L9 (26 DUPLICATES REMOVED)
L11 9525 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))
L12 122 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) ANTIBOD?
L13 67 S L12 AND PD-19980327
L14 42 DUP REM L13 (25 DUPLICATES REMOVED)
L15 0 S L14 (10N) ADMINIST?
L16 0 S L14 (P) ADMINIST?

7
W0 99 47565
98 11435

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NEWS 4 Apr 09 ZDB will be removed from STN
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NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREG no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
 saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 30 NETFIRST to be removed from STN
NEWS 16 Aug 08 CANCERLIT reload
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
 now available on STN
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985

| | |
|--------------|---|
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CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
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=> file medline caplus embase biosis
 COST IN U.S. DOLLARS SINCE FILE TOTAL
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 FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 16:59:34 ON 15 OCT 2002

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FILE 'BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
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=> s rademacher t?/au or whitby h?/au
L1 550 RADEMACHER T?/AU OR WHITBY H?/AU

=> s 11 and (ipg or (inositolphosphoglycans))
L2 47 L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))

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*-> dup rem l2  
PROCESSING COMPLETED FOR L2  
L3          28 DUP REM L2 (19 DUPLICATES REMOVED)
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=> dis l3 1-28 ibib abs

L3 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10305 CAPLUS
DOCUMENT NUMBER: 136:64163
TITLE: Materials and methods relating for the treatment and
diagnosis of pre-eclampsia
INVENTOR(S): Schofield, Julian; Rademacher, Thomas William
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 45 pp.
Coden: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002000254 A2 20020103 WO 2001-GB2800 20010625

WO 2002000254 A3 20020530

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001074330 A5 20020108

AU 2001-74330 20010625

PRIORITY APPLN. INFO.: GB 2000-15625 A 20000626

WO 2001-GB2800 W 20010625

AB The present invention relates to use of GPI-PLD (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial GPI-PLD activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated GPI-PLD activity present in the placenta in pre-eclampsia may be correctable by administration of GPI-PLD to the mother to correct the problems caused by abnormal or dysregulated GPI-PLD, e.g. to reduce the abnormal release and in situ prodn. of placental IPGs (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous GPI-PLD or a fragment thereof, e.g. an inactive GPI-PLD capable of competing with or displacing the abnormal or dysregulated GPI-PLD, e.g. from Apo-A1.

L3 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:833641 CAPLUS

DOCUMENT NUMBER: 135:354965

TITLE: Gelatin in assays, kits and lateral flow devices for determining inositol phosphoglycans and diagnosing pre-eclampsia

INVENTOR(S): Williams, Philip; Bord, Stephanie; Rademacher, Thomas William

PATENT ASSIGNEE(S): Rademacher Group Limited, UK

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2001086292 | A2 | 20011115 | WO 2001-GB2082 | 20010511 |
| WO 2001086292 | A3 | 20020620 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-11590 A 20000512
GB 2001-2566 A 20010201

AB Assays, kits and methods for detg. the presence or amt. inositol phosphoglycans (IPG) analytes in samples are disclosed based on the finding that IPG antigens are capable of binding to gelatin. These assays can be used in the diagnosis of conditions where the presence or amt. of these analytes is a diagnostic marker for a condition. Methods for the diagnosis of pre-eclampsia, distinguishing different type of pre-eclampsia, are disclosed and also methods for detg. the onset of labor in a patient. An ELISA assay was developed using gelatin as the capture agent and rabbit polyclonal anti-IPG sera and a goat anti-rabbit horseradish peroxidase conjugated antibody as a two-component developing agent to analyze pre-eclamptic urine samples.

L3 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:833334 CAPLUS

DOCUMENT NUMBER: 135:358109

TITLE: Preparation of inositol phosphoglycan derivatives as antidiabetics and IPG antagonists

INVENTOR(S): Martin-Lomas, Manuel; Rademacher, Thomas William; Caro, Hugo Roberto; Francois, Irene

PATENT ASSIGNEE(S): Rademacher Group Limited, UK

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2001085747 | A1 | 20011115 | WO 2001-GB2093 | 20010511 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001053767 A1 20011220 US 2001-798125 20010302

PRIORITY APPLN. INFO.: GB 2000-11591 A 20000512

US 2000-203607P F 20000512

US 2001-798125 A 20010302

AB Compds. X-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an inositolphosphoglycan (IPG), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an IPG second messenger or an IPG antagonist thereof.

Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic IPG

-P and/or IPG-A activities mentioned above to det. whether they will be suitable for use a IPG mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, O-(2-amino-2-deoxy-D-glucopyranosyl)-beta.(1,6)-D-3-O-methyl-chiro-inositol was prepd. and used to treat a condition ameliorated by administration of and IPG second messenger or an IPG antagonist.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:833333 CAPLUS
 DOCUMENT NUMBER: 135:344674
 TITLE: Preparation of inositol phosphoglycan derivatives as antidiabetics and IPG antagonists
 INVENTOR(S): Martin-Lomas, Manuel; Rademacher, Thomas William; Caro, Hugo Norberto; Francois, Irene
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 68 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|------------|
| WO 2001085746 | A1 | 20011115 | WO 2001-GB2083 | 20010511 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2001056072 | A1 | 20011227 | US 2001-798124 | 20010302 |
| PRIORITY APPN. INFO.: | | | GB 2000-11592 | A 20000512 |
| | | | US 2000-203599P | P 20000512 |
| | | | US 2001-798124 | A 20010302 |

AB Compds. X-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an inositolphosphoglycan (IPG), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an IPG second messenger or an IPG antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic IPG -P and/or IPG-A activities mentioned above to det. whether they will be suitable for use a IPG mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, 1'-D-6-O-(2'-amino-4'-O-phosphate-2'-deoxy-.alpha.-D-glucopyranosyl)-myo-inositol-1,2-cyclic phosphate was prepd. and used to treat a condition ameliorated by administration of and IPG second messenger or an IPG antagonist.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:833332 CAPLUS
 DOCUMENT NUMBER: 135:358108
 TITLE: Preparation of inositol phosphoglycans as antidiabetics and IPG antagonists
 INVENTOR(S): Rademacher, Thomas William; Caro, Hugo Norberto; Francois, Irene; Martin-Lomas, Manuel
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|------------|
| WO 2001085745 | A1 | 20011115 | WO 2001-GB2098 | 20010511 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2001041677 | A1 | 20011115 | US 2001-798004 | 20010302 |
| PRIORITY APPN. INFO.: | | | GB 2000-11593 | A 20000512 |
| | | | US 2000-203598P | P 20000512 |
| | | | US 2001-798004 | A 20010302 |

AB Compds. having a mimetic or antagonistic property of an inositol phosphoglycan Y-X-cyclitols wherein X and Y are sugar residue, cyclitol is substituted with phosphate, thiophosphate, phosphate ester, phosphonate, thiophosphate ester, thiophosphonate, phosphoramidite, phosphoramide, cyclic phosphate, sulfur group, substituted hydroxyl group, halogen, and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an IPG second messenger or an IPG antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular, the compds. are based on the linkage of two or more sugar residues to a cyclitol. Effect of these compds. on the activity of PDH phosphatase, PDH kinase, and acetyl CoA carboxylase I is reported. Thus, O-.alpha.-D-galactopyranosyl-(1-4)-(2-amino-2-deoxy-.alpha.-D-glucopyranosyl)-(1-6)-D-myoinositol was prepd. and tested as antidiabetics and IPG antagonist.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:833327 CAPLUS
 DOCUMENT NUMBER: 135:358107
 TITLE: Preparation of inositol phosphates to treat a condition ameliorated by administration of and IPG second messenger or an IPG antagonist
 INVENTOR(S): Martin-Lomas, Manuel; Rademacher, Thomas William; Caro, Hugo Norbert; Francois, Irene
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 107 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2001085740 | A2 | 20011115 | WO 2001-GB2088 | 20010511 |
| WO 2001085740 | A3 | 20020328 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2001051606 | A1 | 20011213 | US 2001-798005 | 20010302 |
| AU 2001060426 | A5 | 20011120 | AU 2001-60426 | 20010511 |
| PRIORITY APPLN. INFO.: | | | GB 2000-11594 | A 20000512 |
| | | | US 2000-203596P | P 20000512 |
| | | | US 2001-798005 | A 20010302 |
| | | | US 2000-203599P | P 20000512 |
| | | | WO 2001-GB2088 | W 20010511 |

AB Compds. X-1,6-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an inositolphosphoglycan (IPG), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an IPG second messenger or an IPG antagonist thereof. In particular, the compds. are based on the 1,6 linkage of a sugar residue and a cyclitol. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic IPG-P and/or IPG-A activities mentioned above to det. whether they will be suitable for use as a IPG mimetics or antagonists. Preferred assays measure the effect of the compds. on PDE phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, 1'-D-6-O-(2'-amino-4'-O-phosphate-2'-deoxy-.alpha.-D-glucopyranosyl)-myo-inositol-1,2-cyclic phosphate was prep. and used to treat a condition ameliorated by administration of and IPG second messenger or an IPG antagonist.

L3 ANSWER 7 OF 28 MEDLINE DUPLICATE 1
 ACCESSION NUMBER: 2001412385 MEDLINE
 DOCUMENT NUMBER: 21354778 PubMed ID: 11461192
 TITLE: Reversal of type 2 diabetes in mice by products of malaria parasites. II. Role of inositol phosphoglycans (IPGs).
 AUTHOR: Elased K M; Guma K A; de Souza J B; Rahmoune H; Playfair J H; Rademacher T W
 CORPORATE SOURCE: Rademacher Group Ltd, Arthur Stanley House, 6th Floor, 40-50 Tottenham Street, London W1P 9PG, United Kingdom.. Khalid.elased@rademacher.co.uk
 SOURCE: MOLECULAR GENETICS AND METABOLISM, (2001 Jul) 73 (3) 248-58.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200110
 ENTRY DATE: Entered STN: 20011008
 Last Updated on STN: 20011008
 Entered Medline: 20011004

AB We have previously shown that infection with Plasmodium yoelii malaria or injection of extracts from malaria-parasitized red cells induces hypoglycemia in normal mice and normalizes the hyperglycemia in mice made moderately diabetic with streptozotocin. Inositol phosphoglycans (IPGs) are released outside cells by hydrolysis of membrane-bound glycosylphosphatidylinositols (GPIs), and act as second messengers mediating insulin action. The C57BL/Ks-db/db and C57BL/6J-ob/ob mice offer good models for studies on human obesity and Type 2 diabetes. In the present study, we show that a single iv injection of IPG-A or IPG-P extracted from P. yoelii significantly ($P < 0.02$) lowers the blood glucose in STZ-diabetic, db/db, and in ob/ob mice for at least 4--6 h. Using rat white adipocytes, IPG-P increased lipogenesis by 20--30% in the presence and absence of maximal concentrations of insulin ($10(-8)$ M) ($P < 0.01$) and stimulated pyruvate dehydrogenase (PDH) phosphatase in a dose-related manner. Both IPG-A and IPG-P inhibited c-AMP-dependent protein kinase (PKA) in a dose-related manner. Compositional analysis of IPGs after 24 h hydrolysis revealed the presence of myo-inositol, phosphorus, galactosamine, glucosamine, and glucose in both IPG-A and IPG-P. However, hydrolysis of IPGs for 4 h highlighted differences between IPG-A and IPG-P. There are some functional similarities between P. yoelii IPGs and those previously described for mammalian liver. However, this is the first report of the hypoglycemic effect of IPGs in murine models of Type 2 diabetes. We suggest that IPGs isolated from P. yoelii, when fully characterized, may provide structural information for the synthesis of new drugs for the management of diabetes mellitus.

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L3 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:911091 CAPLUS

DOCUMENT NUMBER: 134:37032
 TITLE: Adenosine diphosphatase and activators thereof and
 their therapeutic and diagnostic uses for preeclampsia
 and platelet aggregation-associated conditions
 INVENTOR(S): McLean, Patricia; Greenbaum, Leslie; Rademacher,
 Thomas William
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2000078330 | A2 | 20001228 | WO 2000-GB2333 | 20000616 |
| WO 2000078330 | A3 | 20010525 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| EP 1185295 | A2 | 20020313 | EP 2000-940550 | 20000616 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |

PRIORITY APPLN. INFO.: GB 1999-14326 A 19990618

WO 2000-GB2333 W 20000616

AB Materials and methods are provided for the diagnosis and treatment of preeclampsia and related conditions characterized by platelet aggregation. Adenosine diphosphatase (ADPase) and activators of ADPase are used for the treatment of preeclampsia, in order to overcome the inhibition of ADPase by inositol phosphoglycans (IPGs). Also provided is a method for screening for compds. with ADPase-stimulatory activity in the presence or absence of IPGs.

L3 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:457304 CAPLUS

DOCUMENT NUMBER: 133:55669

TITLE: Treatment and diagnosis of cancer using

INVENTOR(S): Rademacher, Thomas William; Caro, Hugo

PATENT ASSIGNEE(S): Rademacher Group Limited, UK

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2000039589 | A1 | 20000706 | WO 1999-GB4382 | 19991223 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| EP 1141723 | A1 | 20011010 | EP 1999-962426 | 19991223 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | |

JP 2002533475 T2 20021008 JP 2000-591437 19991223

PRIORITY APPLN. INFO.: GB 1998-28564 A 19981223

WO 1999-GB4382 W 19991223

AB Inositolphosphoglycans (IPGs), and in particular A-type substances comprising myo-inositol, are tumor autocrine factors (TAFs), that is factors which cause tumor cell proliferation. The use of A-type IPG antagonists for the treatment of cancer and a method for the diagnosis or prognosis of cancer based on the presence or amt. of IPGs in a sample from a patient is disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:15024 CAPLUS

DOCUMENT NUMBER: 132:59168

TITLE: Inositolphosphoglycan and ribose for treatment of ischemia-reperfusion injury

INVENTOR(S): Rademacher, Thomas William; Greenbaum, Leslie; McLean, Patricia

PATENT ASSIGNEE(S): University College London, UK

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2000000205 | A1 | 20000106 | WO 1999-GB1499 | 19990512 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 9939402 | A1 | 20000117 | AU 1999-39402 | 19990512 |
| AU 748892 | B2 | 20020613 | | |
| EP 1091743 | A1 | 20010418 | EP 1999-922293 | 19990512 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |

JP 2002519328 T2 20020702 JP 2000-556790 19990512
PRIORITY APPLN. INFO.: GB 1998-14039 A 19980629
WO 1999-GB1499 W 19990512

AB Compns. comprising inositolphosphoglycans (IPGs) and ribose are disclosed, and their use in the prevention or treatment of ischemic-reperfusion injury. This treatment increases the energy generating systems of cells by employing the mitochondrial oxidative restoration system. The use of the compns. in preserving organs for transplantation is also disclosed.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 28 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2000513875 MEDLINE
DOCUMENT NUMBER: 20522979 PubMed ID: 11072827
TITLE: Inositolphosphoglycan mediators structurally related to glycosyl phosphatidylinositol anchors: synthesis, structure and biological activity.
AUTHOR: Martin-Lomas M; Khiar N; Garcia S; Kessler J L; Nieto P M; Rademacher T W
CORPORATE SOURCE: Grupo de Carbohidratos, Instituto de Investigaciones Químicas CSIC-UNSE, Sevilla, Spain.. manuel.martin-lomas@iq.cartuja.csic.es
SOURCE: CHEMISTRY, (2000 Oct 2) 6 (19) 3608-21.
Journal code: 9513783. ISSN: 0947-6539.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001128

AB The preparation of the pseudopentasaccharide 1a, an inositol-phosphoglycan (IPG) that contains the conserved linear structure of glycosyl phosphatidylinositol anchors (GPI anchors), was carried out by using a highly convergent 2+3-block synthesis approach which involves imidate and sulfoxide glycosylation reactions. The preferred solution conformation of this structure was determined by using NMR spectroscopy and molecular dynamics simulations prior to carrying out quantitative structure-activity relationship studies in connection with the insulin signalling process. The ability of 1a to stimulate lipogenesis in rat adipocytes as well as to inhibit cAMP dependent protein kinase and to activate pyruvate dehydrogenase phosphatase was investigated. Compound 1a did not show any significant activity, which may be taken as a strong indication that the GPI anchors are not the precursors of the IPG mediators.

L3 ANSWER 12 OF 28 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 2000188034 MEDLINE
DOCUMENT NUMBER: 20188034 PubMed ID: 10720442
TITLE: Inositol phosphoglycans and signal transduction systems in pregnancy in preeclampsia and diabetes: evidence for a significant regulatory role in preeclampsia at placental and systemic levels.
AUTHOR: Kunjara S; Greenbaum A L; Wang D Y; Caro H N; McLean P; Redman C W; Rademacher T W
CORPORATE SOURCE: Department of Molecular Pathology, Molecular Medicine Unit, The Windeyer Building, 46, University College London Medical School, Cleveland Street, London, W1P 6DB, England.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (2000 Feb) 69 (2) 144-58.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000606
Last Updated on STN: 20000606
Entered Medline: 20000519

AB Measurements have been made of the urinary content of inositol phosphoglycans IPG P-type and IPG A-type, putative insulin second messengers, in preeclampsia, in type I insulin-treated diabetic pregnant women and their matched control subjects, and nonpregnant women of child-bearing age. The content of IPG P-type and IPG A-type was also measured in the placenta from preeclamptic patients and from normal pregnancies. Pregnancy was associated with an increase, approximately twofold, in urinary output of IPG-P-type relative to nonpregnant controls ($P<0.01$). The 24-h output of IPG P-type in urine in preeclamptic women was significantly higher (2- to 3-fold) than in pregnant control subjects matched for age, parity, and stage of gestation ($P<0.02$). In contrast, insulin-dependent diabetic pregnant women did not show any significant change in urinary output of IPG P-type or IPG A-type relative to pregnant control subjects. Evidence for a possible relationship and correlation between the urinary excretion of IPG P-type and markers of preeclampsia, including proteinuria ($r = 0.720$, $P<0.01$), plasma aspartate transaminase ($r = 0.658$, $P<0.05$), and platelet counts ($r = 0.613$, $P<0.05$) is presented. A high yield of IPG P-type was extracted from human placenta, in preeclampsia some 3-fold higher ($P < 0.03$) than the normal value, whereas no IPG A-type (with lipogenic-stimulating activity) was found. Low concentrations of placental IPG A-type were detected relative to IPG P-type using assay systems dependent upon the effect of this mediator on cAMP-dependent protein kinase or on a proliferation assay using thymidine incorporation into DNA of EGFR T17 fibroblasts. It is postulated that the high urinary excretion IPG P-type in preeclampsia reflects high placental levels and relates to the accumulation of glycogen in the placenta. The paracrine effects of placental IPG P-type (stimulation off other endocrine glands and/or endothelial cells) could contribute to the pathogenesis of the maternal syndrome. A possible theoretical link between elevated placental IPG P-type and apoptosis is proposed.
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L3 ANSWER 13 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:50486 BIOSIS
DOCUMENT NUMBER: PREV200100050486
TITLE: Inositol phosphoglycans (IPGs) derived from Plasmodium yoelii mimic insulin action in vivo.
AUTHOR(S): Elased, K. M. (1); Gumaa, K. A. (1); de Souza, J. B.; Rademacher, T. W.

CORPORATE SOURCE: (1) Rademacher Group Ltd, 40-50 Tottenham Street, Arthur Stanley House, 6th Floor, London, W1P 9PG UK
 SOURCE: Journal of Endocrinology, (November, 2000) Vol. 167, No. Supplement, pp. P62. print.
 Meeting Info.: 191st Meeting of the Society for Endocrinology London, England, UK November 20-21, 2000
 Society for Endocrinology . ISSN: 0022-0795.

DOCUMENT TYPE: Conference
 LANGUAGE: English
 SUMMARY LANGUAGE: English

L3 ANSWER 14 OF 28 MEDLINE DUPLICATE 4
 ACCESSION NUMBER: 200295348 MEDLINE
 DOCUMENT NUMBER: 20295348 PubMed ID: 10833332
 TITLE: Inositol phosphoglycans and the regulation of the secretion of leptin: in vitro effects on leptin release from adipocytes and the relationship to obesity.
 AUTHOR: Kunjara S; Wang D Y; McLean P; Greenbaum A L;
 Rademacher T W
 CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, UK.
 SOURCE: MOLECULAR GENETICS AND METABOLISM, (2000 May) 70 (1) 61-8.
 Journal code: 9805456. ISSN: 1096-7192.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200007
 ENTRY DATE: Entered STN: 20000728
 Last Updated on STN: 20000728
 Entered Medline: 20000719

AB The ratio of two families of inositol phosphoglycans (IPG-A: IPG-P), insulin second messengers, is raised in non-insulin-dependent diabetes mellitus (NIDDM) and obesity. It is shown here that IPG A type inhibits leptin release from adipocytes, contrasting with the action of insulin (stimulation) and IPG P type (no effect). The significance of inhibitory effects of IPG A type on leptin release is important in relation to obesity and NIDDM in view of the action of leptin in promoting Lep expression and fat oxidation in muscle, in addition to its effects on satiety. Energy conservation and oxidation via interorgan regulation by leptin could be compromised by a rise in the IPG-A:IPG-P ratio.
 Copyright 2000 Academic Press.

L3 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:640696 CAPLUS
 DOCUMENT NUMBER: 131:256346
 TITLE: Antagonism of inositolphosphoglycan signaling in mast cells, basophils and eosinophils
 INVENTOR(S): Rademacher, Thomas William; Whitby, Helen
 PATENT ASSIGNEE(S): University College London, UK
 SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9949855 | A2 | 19991007 | WO 1999-GB981 | 19990329 |
| WO 9949855 | A3 | 19991118 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2319588 | AA | 19991007 | CA 1999-2319588 | 19990329 |
| AU 9931596 | A1 | 19991018 | AU 1999-31596 | 19990329 |
| EP 1066043 | A2 | 20010110 | EP 1999-913481 | 19990329 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

PRIORITY APPLN. INFO.: GB 1998-6645 A 19980327
 WO 1999-GB981 W 19990329

AB The authors disclose that inositolphosphoglycans (IPGs) can be obtained from basophils, eosinophils and mast cells and that allergen stimulation of these cells results in IPG release. IPGs, acting as second messengers in non-allergen stimulated cells, induced histamine release or degranulation. Thus, IPG antagonists are envisioned for the treatment of conditions (esp. allergy and asthma) mediated by the release of IPGs from mast cells, basophils or eosinophils. Preferred IPG antagonists include anti-IPG antibodies, inhibitors of the enzyme glycosylphosphatidylinositol phospholipase D, and competitive antagonists.

L3 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:614255 CAPLUS
 DOCUMENT NUMBER: 131:237961
 TITLE: Materials and methods using antibody binding for identifying inositolphosphoglycan mimetics
 INVENTOR(S): Rademacher, Thomas William; Williams, Phillip
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9947926 | A2 | 19990923 | WO 1999-GB845 | 19990318 |
| WO 9947926 | A3 | 19991104 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, | | | | |

MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
 TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
 MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2321734 AA 19990923 CA 1999-2321734 19990318
 AU 9929468 A1 19991011 AU 1999-29468 19990318
 EP 1066521 A2 20010110 EP 1999-910536 19990318
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 JP 2002507724 T2 20020312 JP 2000-537070 19990318

PRIORITY APPLN. INFO.: GB 1998-5771 A 19980318
 WO 1999-GB845 W 19990318
AB Methods for detg. a binding profile for an inositolphosphoglycan (IPG) or a candidate mimetic compd. are disclosed in which the IPG or candidate mimetic compd. is contacted with an anti-IPG antibody in binding assay and the binding of the IPG or candidate mimetic compd. to the antibody is used to establish the binding profiles. The profiles are then used in methods for identifying candidate compds. for further testing or development as IPG mimetics, providing lead compds. for further development as pharmaceuticals.

L3 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:613973 CAPLUS
 DOCUMENT NUMBER: 131:241984
 TITLE: Anti-inositolphosphoglycan monoclonal antibodies
 INVENTOR(S): Nieto, Isabel Varela; Mato, Jose; Prieto, Jesus;
 Williams, Phillip; Rademacher, Thomas William
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 65 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|------------|--------------------------|--------------------------|
| WO 9947565 | A1 | 19990923 | WO 1999-GB844 | 19990318 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KR, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | CA 2321113 | AA 19990923 | CA 1999-2321113 19990318 |
| AU 9929467 | A1 | 19991011 | AU 1999-29467 | 19990318 |
| AU 748080 | B2 | 20020530 | | |
| EP 1062246 | A1 | 20001227 | EP 1999-910535 | 19990318 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002506631 | T2 | 20020305 | JP 2000-536756 | 19990318 |
| PRIORITY APPLN. INFO.: GB 1998-5739 A 19980318 | | | | |
| | | | GB 1998-11000 A 19980521 | |
| | | | WO 1999-GB844 W 19990318 | |

AB The present invention relates to anti-IPG antibodies, and in particular monoclonal antibodies produced by hybridoma cell lines 2F7, 2D1 and 5H6, and the use of these and other similar antibodies in the treatment and diagnosis of pre-eclampsia or diabetes, esp. type I diabetes. A method of producing anti-IPG antibodies by immunizing an animal with IPG unconjugated to an immunogenic carrier is also disclosed.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:495179 CAPLUS
 DOCUMENT NUMBER: 131:125475
 TITLE: Neurotrophic properties of IPGs and IPG analogues
 INVENTOR(S): Rademacher, Thomas William; Caro, Hugo Norberto; Martin-Lomas, Manuel; Nieto, Isabel Varela; Alvarez, Yolanda Leon
 PATENT ASSIGNEE(S): Rademacher Group Limited, UK
 SOURCE: PCT Int. Appl., 30 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|------------|---------------------------|--------------------------|
| WO 9938516 | A1 | 19990805 | WO 1998-GB3847 | 19981221 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | CA 2318584 | AA 19990805 | CA 1998-2318584 19981221 |
| AU 9917708 | A1 | 19990816 | AU 1999-17708 | 19981221 |
| EP 1064003 | A1 | 20010103 | EP 1998-962574 | 19981221 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002501899 | T2 | 20020122 | JP 2000-529249 | 19981221 |
| PRIORITY APPLN. INFO.: GB 1998-1899 A 19980129 | | | | |
| | | | WO 1998-GB3847 W 19981221 | |

AB Inositolphosphoglycans (IPGs) or inositol-contg. IPG analogs can be used to specifically cause neuron proliferation or neuron differentiation, and in particular neurite outgrowth. P-type IPGs or chiro-inositol contg. analogs cause neurite outgrowth and A-type IPGs or myo-inositol contg. analogs cause neuron proliferation. Compns. comprising these agents and their medical uses are also disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 28 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000076804 MEDLINE
DOCUMENT NUMBER: 20076804 PubMed ID: 10607479
TITLE: Inositol phosphoglycans in diabetes and obesity: urinary levels of IPG A-type and IPG P-type, and relationship to pathophysiological changes.
AUTHOR: Kunjara S; Wang D Y; Greenbaum A L; McLean P; Kurtz A; Rademacher T W
CORPORATE SOURCE: Department of Molecular Pathology, Molecular Medicine Unit, University College London Medical School, The Windeyer Building, 46, Cleveland Street, London, W1P 6DB, United Kingdom.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (1999 Dec) 68 (4) 488-502.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000301

AB Measurements have been made, in adult male diabetic patients and control subjects, of the urinary content of inositol phosphoglycans (IPGs), the IPG A-type and IPG P-type forms, which, among other actions, regulate pathways of glucose utilization, lipogenesis, triglyceride formation, and pyruvate dehydrogenase (PDH) activity. Urine samples from the entire diabetic group showed a 2- to 3-fold increase in IPG A-type, and a fall in the IPG P-type:IPG A-type ratio relative to the control group. Subdivision of the diabetic patients into lean IDDM and obese NIDDM groups revealed significant differences in the IPG P-type:IPG A-type ratio between these groups, this ratio decreasing with increases in the body mass index (BMI). Analysis of the relationships among IPGs and HbA1, blood pressure, and BMI indicated that a fall in the IPG P-type:IPG A-type ratio correlated with a rise in the HbA1 (indicative of impaired glycemic control), with increased systolic blood pressure and increased obesity, all factors linked to Syndrome X. There was a parallelism between the profile of the IPG P-type:IPG A-type ratio and the well-established pattern of insulin resistance and BMI. In vitro studies of the effects of alterations in the IPG P-type:IPG A-type ratio on the activation of the pyruvate dehydrogenase complex (PDH complex) at the PDH phosphatase reaction demonstrated that IPG A-type forms antagonized the stimulation of the PDH phosphatase by IPG P-type forms, thus having a negative effect on the conversion of PDH to the active, dephosphorylated, form. This observation could provide a mechanism whereby the shifts in the IPG P-type:IPG A-type ratio reported above could change the metabolic pattern from one directed to glucose oxidation to one more directed toward energy conservation and lipid storage.

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L3 ANSWER 20 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:393699 BIOSIS
DOCUMENT NUMBER: PREV199900393699
TITLE: Higher detection of inositolphosphoglycans (IPG) in pre-eclamptic than in normal placenta by immunohistochemical staining.
AUTHOR(S): Debordé, S. (1); Sooranna, S. R.; Williams, P. J. (1); Mato, J.; Rademacher, T. W. (1)
CORPORATE SOURCE: (1) Molecular Medicine Unit, Department of Molecular Pathology, UCL, London UK
SOURCE: Placenta, (July-Aug., 1999) Vol. 20, No. 5-6, pp. A.21. Meeting Info.: 5th Conference of the International Federation of Placenta Associations and the 8th Meeting of the European Placenta Group Schladming, Austria September 26-29, 1999 European Placenta Group . ISSN: 0143-4004.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:393697 BIOSIS
DOCUMENT NUMBER: PREV199900393697
TITLE: Investigation of inositolphosphoglycans (IPG) activity in the brush border membrane of normal and pre-eclamptic (PE) human placenta.
AUTHOR(S): Debordé, S. (1); Kunjara, S. (1); Rademacher, T. W. (1)
CORPORATE SOURCE: (1) Mol Med Unit, Department of Molecular Pathology, UCL, London UK
SOURCE: Placenta, (July-Aug., 1999) Vol. 20, No. 5-6, pp. A.20. Meeting Info.: 5th Conference of the International Federation of Placenta Associations and the 8th Meeting of the European Placenta Group Schladming, Austria September 26-29, 1999 European Placenta Group . ISSN: 0143-4004.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:184077 CAPLUS
DOCUMENT NUMBER: 128:226252
TITLE: Materials and methods using P- and A-type inositolphosphoglycans and their antagonists for the diagnosis and treatment of diabetes and associated obesity
INVENTOR(S): Rademacher, Thomas William; McLean, Patricia
PATENT ASSIGNEE(S): Hoeft Rademacher Limited, UK; Rademacher, Thomas William; McLean, Patricia
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXDD
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

WO 9811435 A1 19980319 WO 1997-GB2440 19970911
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
 KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
 NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
 US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
 GN, ML, MR, NE, SN, TD, TG
 AU 9741304 A1 19980402 AU 1997-41304 19970911
 AU 722425 B2 20000803
 EP 925503 A1 19990630 EP 1997-939083 19970911
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 CN 1234118 A 19991103 CN 1997-199097 19970911
 BR 9711753 A 20000118 BR 1997-11753 19970911
 JP 2001505658 T2 20010424 JP 1998-513366 19970911
 PRIORITY APPLN. INFO.: GB 1996-18934 A 19960911
 WO 1997-GB2440 W 19970911

AB The diagnosis of diabetes based on the level or ratio of P- and A-type inositolphosphoglycans (IPGs) in a sample from a patient, and the use of P- and A-type IPGs or their antagonists in the treatment of diabetes, are disclosed. In particular, the invention provides treatment of IDDM or lean type II diabetes (NIDDM) with a mixt. of P- and A-type mediators, and treatment of obese type II diabetes (NIDDM) with a P-type mediator and/or an A-type antagonist.

L3 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:180889 CAPLUS
 DOCUMENT NUMBER: 128:240997
 TITLE: Cyclitol containing carbohydrates from human tissue which regulate glycogen metabolism and their use in pharmaceuticals
 INVENTOR(S): Rademacher, Thomas William; Caro, Hugo
 PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
 SOURCE: PCT Int. Appl., 64 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9811117 | A1 | 19980319 | WO 1997-GB2533 | 19970911 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9743101 | A1 | 19980402 | AU 1997-43101 | 19970911 |
| AU 713100 | B2 | 19991125 | | |
| EP 925304 | A1 | 19990630 | EP 1997-919168 | 19970911 |
| EP 925304 | B1 | 20000426 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI | | | | |
| AT 192160 | E | 20000515 | AT 1997-919168 | 19970911 |
| ES 2147988 | T3 | 20001001 | ES 1997-919168 | 19970911 |
| JP 2001500859 | T2 | 20010123 | JP 1998-513410 | 19970911 |
| US 6271204 | B1 | 20010807 | US 1999-254748 | 19990614 |
| PRIORITY APPLN. INFO.: | | | GB 1996-18929 | A 19960911 |
| | | | WO 1997-GB2533 | W 19970911 |

AB The application relates to the purifn. and characterization of a family of P-type inositolphosphoglycans (IPGs) from human liver and placenta. These substances are shown to have P-type biol. activity, e.g., activating pyruvate dehydrogenase (PDH) phosphatase. The characterization of the compds. demonstrates that they contain metal ions, in particular Mn²⁺ and/or Zn²⁺, and optionally phosphate. The compds. and their antagonists have used as pharmaceuticals, e.g., for the treatment of diabetes, and in screening for synthetic analogs.

L3 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:180888 CAPLUS
 DOCUMENT NUMBER: 128:242350
 TITLE: A type A glycosylinositol second messenger from human tissue involve in regulation of lipogenesis
 INVENTOR(S): Rademacher, Thomas William; Caro, Hugo
 PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
 SOURCE: PCT Int. Appl., 62 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9811116 | A1 | 19980319 | WO 1997-GB2444 | 19970911 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9741307 | A1 | 19980402 | AU 1997-41307 | 19970911 |
| AU 713103 | B2 | 19991125 | | |
| EP 925305 | A1 | 19990630 | EP 1997-939087 | 19970911 |
| EP 925305 | B1 | 20000426 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI | | | | |
| AT 192161 | E | 20000515 | AT 1997-939087 | 19970911 |
| ES 2147996 | T3 | 20001001 | ES 1997-939087 | 19970911 |
| JP 2001504450 | T2 | 20010403 | JP 1998-513368 | 19970911 |
| US 6303580 | B1 | 20011016 | US 1999-254797 | 19990604 |
| US 2001039027 | A1 | 20011108 | US 2001-775856 | 20010201 |
| PRIORITY APPLN. INFO.: | | | GB 1996-18930 | A 19960911 |

AB A family of A-type inositolphosphoglycans (IPGs) from human liver and placenta that appear to play a role in the regulation of lipogenesis are identified and characterized. These substances have the biol. activity assocd. with A-type IPG fractions, namely regulating lipogenic activity and inhibiting cAMP dependent protein kinase. The characterization of the compds. demonstrates that they contain metal ions, in particular Zn²⁺, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g. for the treatment of diabetes, and in screening for synthetic analogs.

L3 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:180785 CAPLUS

DOCUMENT NUMBER: 128:226268

TITLE: P-type inositolphosphoglycans and antagonists thereof in diagnosis and treatment of pre-eclampsia and diabetes

INVENTOR(S): Rademacher, Thomas William; Mclean, Patricia

PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Mclean, Patricia

SOURCE: PCT Int. Appl., 63 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9810791 | A1 | 19980319 | WO 1997-GB2534 | 19970911 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BE, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9743102 | A1 | 19980402 | AU 1997-43102 | 19970911 |
| AU 715884 | B2 | 20000210 | | |
| EP 939651 | A1 | 19990908 | EP 1997-919169 | 19970911 |
| EP 939651 | B1 | 20000531 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1235556 | A | 19991117 | CN 1997-199318 | 19970911 |
| BR 9711752 | A | 20000118 | BR 1997-11752 | 19970911 |
| AT 193452 | E | 20000615 | AT 1997-919169 | 19970911 |
| ES 2148967 | T3 | 20001016 | ES 1997-919169 | 19970911 |
| JP 2001501598 | T2 | 20010206 | JP 1998-513411 | 19970911 |
| PRIORITY APPLN. INFO.: | | | GB 1996-18931 | A 19960911 |
| | | | WO 1997-GB2534 | W 19970911 |

AB The invention relates to materials and methods for the diagnosis and treatment of pre-eclampsia, and more particularly to the role of P-type inositolphosphoglycans (IPGs) in the occurrence of pre-eclampsia. Methods of diagnosing pre-eclampsia by detg. the level of P-type IPGs and uses of antagonists of P-type IPGs in the treatment of pre-eclampsia are disclosed, together with a method for screening for P-type IPG antagonists.

L3 ANSWER 26 OF 28 MEDLINE DUPLICATE 6

ACCESSION NUMBER: 97406564 MEDLINE

DOCUMENT NUMBER: 97406564 PubMed ID: 9259987

TITLE: Isolation and partial characterisation of insulin-mimetic inositol phosphoglycans from human liver.

AUTHOR: Caro H N; Kunjara S; Rademacher T W; Leon Y;

Jones D R; Avila M A; Varela-Nieto I

CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, United Kingdom.

SOURCE: BIOCHEMICAL AND MOLECULAR MEDICINE, (1997 Aug) 61 (2) 214-28.

JOURNAL CODE: 9508702. ISSN: 1077-3150.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199710

ENTRY DATE: Entered STN: 19971105

Last Updated on STN: 20000303

Entered Medline: 19971023

AB Extracts of human liver were found to contain activities which copurified and coeluted with the two major subtypes of mediators (type A and type P) isolated from insulin-stimulated rat liver. The putative type A mediator from human liver inhibited cAMP-dependent protein kinase from bovine heart, decreased phosphoenolpyruvate carboxykinase mRNA levels in rat hepatoma cells, and stimulated lipogenesis in rat adipocytes. The putative type P mediator stimulated bovine heart pyruvate dehydrogenase phosphatase. Both fractions were able to stimulate proliferation of EGFR T17 fibroblasts and the type A was able to support growth in organotypic cultures of chicken embryo cochleovestibular ganglia. Both activities were resistant to Pronase treatment and the presence of carbohydrates, phosphate, and free-amino groups were confirmed in the two fractions. These properties are consistent with the structure/ function characteristics of the type A and P inositolphosphoglycans (IPG) previously characterized from rat liver. Further, the ability of the human-derived mediators to interact with rat adipocytes and bovine-derived metabolic enzymes suggests similarity in structure between the mediators purified from different species. Galactose oxidase-susceptible membrane-associated glycosylphosphatidylinositols (GPI) have been proposed to be the precursors of IPG. GPI was purified from human liver membranes followed by treatment with galactose oxidase and reduction with NaBH₄. Serial t.l.c. revealed three radiolabeled bands which comigrated with the putative GPI precursors found in rat liver. These galactose-oxidase-reactive lipidic compounds, however, were only partially susceptible to hydrolysis with phosphatidylinositol-specific phospholipase C from *Bacillus thuringiensis* and were resistant to glycosylphosphatidylinositol-specific phospholipase C from *Trypanosoma brucei*. These data indicate that IPG molecules with insulin-like biological activities are present in human liver.

L3 ANSWER 27 OF 28 MEDLINE DUPLICATE 7

ACCESSION NUMBER: 96333396 MEDLINE

DOCUMENT NUMBER: 96333396 PubMed ID: 8757890

TITLE: Structural similarities among malaria toxins insulin second messengers, and bacterial endotoxin.
 AUTHOR: Caro H N; Sheikh N A; Taverne J; Playfair J H;
Rademacher T W
 CORPORATE SOURCE: Molecular Medicine Unit, Department of Molecular Pathology,
 University College London Medical School, United Kingdom.
 SOURCE: INFECTION AND IMMUNITY, (1996 Aug) 64 (8) 3438-41.
 Journal code: 0246127. ISSN: 0019-9567.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199609
 ENTRY DATE: Entered STN: 19961008
 Last Updated on STN: 19970203
 Entered Medline: 19960926

AB Malaria toxin causes hypoglycemia and induction of tumor necrosis factor. Extracts of parasitized erythrocytes which were coeluted and copurified with one of the two subtypes of mammalian insulin-mimetic inositolphosphoglycans similarly induced fibroblast proliferation in the absence of serum. In addition, induction of tumor necrosis factor in macrophages by malaria toxin and by lipopolysaccharide from Escherichia coli was enhanced by pretreatment of these toxins with alpha-galactosidase. Thus, parasitized erythrocytes contain both soluble inositolphosphoglycan-like insulin second messengers and endotoxin-like lipidic molecules.

L3 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:315887 CAPLUS
 DOCUMENT NUMBER: 120:315887
 TITLE: Inositolphosphoglycan second messengers
 AUTHOR(S): Rademacher, T. W.; Caro, H.; Kunjara, S.;
 Wang, D. Y.; Greenbaum, A. L.; McLean, P.
 CORPORATE SOURCE: Dep. Mol. Pathol., Univ. Coll. London Med. Sch.,
 London, W1P 6DB, UK
 SOURCE: Brazilian Journal of Medical and Biological Research
 (1994), 27(2), 327-41
 CODEN: BJMRDK; ISSN: 0100-879X
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review, with 77 refs., of the role of inositolphosphoglycan (IPG) in signal transduction by growth factors with special emphasis on insulin and insulin-like factors. Specific topics discussed were: origin of the IPG precursors-glycosylphosphatidylinositol glycans, viz. target cell synthesis vs. circulating hormone vs. membrane-anchored protein; location of IPG generation; relationship to the novel calcium-influx factors; relationship to the insulin-mimetics derived from malarial toxic antigen; relationship to tyrosine kinases and G-proteins; enzymes involved in cell surface GPI hydrolysis; and structure of IPGs.

=> dis his

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
 L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
 L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCAN))
 L3 28 DUP REM L2 (19 DUPLICATES REMOVED)

=> s l3 and GPI-PLD
 L4 1 L3 AND GPI-PLD

=> dis l4 ibib abs kwic

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:10305 CAPLUS
 DOCUMENT NUMBER: 136:64163
 TITLE: Materials and methods relating for the treatment and
 diagnosis of pre-eclampsia
 INVENTOR(S): Schofield, Julian; Rademacher, Thomas William
 PATENT ASSIGNEE(S): University College London, UK
 SOURCE: PCT Int. Appl., 45 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-----------------|------------|
| WO 2002000254 | A2 | 20020103 | WO 2001-GB2800 | 20010625 |
| WO 2002000254 | A3 | 20020530 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2001074330 | A5 | 20020108 | AU 2001-74330 | 20010625 |
| PRIORITY APPLN. INFO.: | | | GB 2000-15625 | A 20000626 |
| | | | WO 2001-GB2800 | W 20010625 |

AB The present invention relates to use of GPI-PLD (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial GPI-PLD activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated GPI-PLD activity present in the placenta in pre-eclampsia may be correctable by administration of GPI-PLD to the mother to correct the problems caused by abnormal or dysregulated GPI-PLD, e.g. to reduce the abnormal release and in situ prodn. of placental IPGs (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous GPI-PLD or a fragment thereof, e.g. an inactive GPI-PLD capable of competing with or displacing the abnormal or dysregulated GPI-PLD, e.g. from Apo-A1.

IN Schofield, Julian; Rademacher, Thomas William

AB The present invention relates to use of GPI-PLD (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial GPI-PLD activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated GPI-PLD activity present in the placenta in pre-eclampsia may be correctable by administration of GPI-PLD to the mother to correct the problems caused by abnormal or dysregulated GPI-PLD, e.g. to reduce the abnormal release and in situ prodn. of placental IPGs (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous GPI-PLD or a fragment thereof, e.g. an inactive GPI-PLD capable of competing with or displacing the abnormal or dysregulated GPI-PLD, e.g. from Apo-A1.

IT Apolipoproteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I, GPI-PLD displacement from; materials and methods relating for the treatment and diagnosis of pre-eclampsia)

=> dis his

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002

L1 550 S RADEMACHE T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
L4 1 S L3 AND GPI-PLD

=> s s (ipg or (inositolphosphoglycans))

MISSING OPERATOR 'S (IPG'

The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s (ipg or (inositolphosphoglycan?))
L5 1504 (IPG OR (INOSITOLPHOSPHOGLYCAN?))

=> s 15 (P) (GPI-PLD or (glycosylphosphatidylinositol phospholipase D))

UNMATCHED LEFT PARENTHESIS 'P' (GPI-PLD'

The number of right parentheses in a query must be equal to the number of left parentheses.

=> s 15 (P) (GPI-PLD or (glycosylphosphatidylinositol (1N) phospholipase D))
L6 4 L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSPHOLI
PASE D))

=> dup rem 16

PROCESSING COMPLETED FOR L6

L7 3 DUP REM L6 (1 DUPLICATE REMOVED)

=> dis 17 1-3 ibib abs

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10305 CAPLUS
DOCUMENT NUMBER: 136:64163
TITLE: Materials and methods relating for the treatment and diagnosis of pre-eclampsia
INVENTOR(S): Schofield, Julian; Rademacher, Thomas William
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXKD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 200200254 | A2 | 20020103 | WO 2001-GB2800 | 20010625 |
| WO 200200254 | A3 | 20020530 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001074330 | A5 | 20020108 | AU 2001-74330 | 20010625 |
| PRIORITY APPLN. INFO.: | | | GB 2000-15625 | A 20000626 |
| | | | WO 2001-GB2800 | W 20010625 |

AB The present invention relates to use of GPI-PLD (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial GPI-PLD activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated GPI-PLD activity present in the placenta in pre-eclampsia may be correctable by administration of GPI-PLD to the mother to correct the problems caused by abnormal or dysregulated GPI-PLD, e.g. to reduce the abnormal release and in situ prodn. of placental IPGs (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous GPI-PLD or a fragment thereof, e.g. an inactive GPI-PLD capable of competing with or displacing the abnormal or dysregulated GPI-PLD, e.g. from Apo-A1.

L7 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001608363 MEDLINE
DOCUMENT NUMBER: 21539556 PubMed ID: 11683370
TITLE: Purification and characterization of insulin-mimetic inositol phosphoglycan-like molecules from grass pea (*Lathyrus sativus*) seeds.
AUTHOR: Paneda C; Villar A V; Alonso A; Goni F M; Varela F; Brodbeck U; Leon Y; Varela-Nieto I; Jones D R
CORPORATE SOURCE: Instituto de Investigaciones Biomedicas Alberto Sols (C.S.I.C.), Madrid, Spain.
SOURCE: MOLECULAR MEDICINE, (2001 Jul) 7 (7) 454-60.

PUB. COUNTRY: Journal code: 9501023. ISSN: 1076-1551.
 DOCUMENT TYPE: United States
 LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
 FILE SEGMENT: English
 ENTRY MONTH: Priority Journals
 200202
 ENTRY DATE: Entered STN: 20011102
 Last Updated on STN: 20020209
 Entered Medline: 20020208

AB BACKGROUND: Signal transduction through the hydrolysis of glycosyl-phosphatidylinositol (GPI) leading to the release of the water-soluble inositol phosphoglycan (IPG) molecules has been demonstrated to be important for mediating some of the actions of insulin and insulin-like growth factor-I (IGF-I). MATERIALS AND METHODS: In the present study, GPI from grass pea (*Lathyrus sativus*) seeds has been purified and partially characterized on the basis of its chromatographic properties and its compositional analysis. RESULTS: The results indicate that it shows similarities to GPI previously isolated from other sources such as rat liver. IPG was generated from *L. sativus* seed GPI by hydrolysis with a GPI-specific phospholipase D (GPI-PLD). This IPG inhibited protein kinase A (PKA) in an *in vitro* assay, caused cell proliferation in explanted cochleovestibular ganglia (CVG), and decreased 8-Br-cAMP-induced phosphoenolpyruvate carboxykinase (PEPCK) mRNA expression in cultured hepatoma cells. CONCLUSIONS: Our data indicate that *L. sativus* seed IPG possess insulin-mimetic activities. This may explain why *L. sativus* seeds have been used in some traditional medicines to ameliorate diabetic symptoms.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:640696 CAPLUS
 DOCUMENT NUMBER: 131:256346
 TITLE: Antagonism of inositolphosphoglycan signaling in mast cells, basophils and eosinophils
 INVENTOR(S): Rademacher, Thomas William; Whitby, Helen
 PATENT ASSIGNEE(S): University College London, UK
 SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 9949855 | A2 | 19991007 | WO 1999-GB981 | 19990329 |
| WO 9949855 | A3 | 19991118 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2319588 | AA | 19991007 | CA 1999-2319588 | 19990329 |
| AU 9931596 | A1 | 19991018 | AU 1999-31596 | 19990329 |
| EP 1066043 | A2 | 20010110 | EP 1999-913481 | 19990329 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| PRIORITY APPLN. INFO.: | | | GB 1998-6645 | A 19980327 |
| | | | WO 1999-GB981 | W 19990329 |

AB The authors disclose that inositolphosphoglycans (IPGs) can be obtained from basophils, eosinophils and mast cells and that allergen stimulation of these cells results in IPG release. IPGs, acting as second messengers in non-allergen stimulated cells, induced histamine release or degranulation. Thus, IPG antagonists are envisioned for the treatment of conditions (esp. allergy and asthma) mediated by the release of IPGs from mast cells, basophils or eosinophils. Preferred IPG antagonists include anti-IPG antibodies, inhibitors of the enzyme glycosylphosphatidylinositol phospholipase D, and competitive antagonists.

=> dis his

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
 L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
 L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCAN*))
 L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
 L4 1 S L3 AND GPI-PLD
 L5 1504 S (IPG OR (INOSITOLPHOSPHOGLYCAN?))
 L6 4 S L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
 L7 3 DUP REM L6 (1 DUPLICATE REMOVED)

=> s 15 (10N) antibod?
 L8 80 L5 (10N) ANTIBOD?

=> s 18 and pd<19980327
 '19980327' NOT A VALID FIELD CODE
 3 FILES SEARCHED...

L9 51 L8 AND PD<19980327

=> dup rem 19
 PROCESSING COMPLETED FOR L9
 L10 25 DUP REM L9 (26 DUPLICATES REMOVED)

=> dis l10 1-25 ibib abs

L10 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:184077 CAPLUS
 DOCUMENT NUMBER: 128:226252
 TITLE: Materials and methods using P- and A-type inositolphosphoglycans and their antagonists for the diagnosis and treatment of diabetes and associated obesity
 INVENTOR(S): Rademacher, Thomas William; McLean, Patricia
 PATENT ASSIGNEE(S): Hoeft Rademacher Limited, UK; Rademacher, Thomas William; McLean, Patricia
 SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|------------------|--------------|
| WO 9811435 | A1 | 19980319 | WO 1997-GB2440 | 19970911 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| AU 9741304 | A1 | 19980402 | AU 1997-41304 | 19970911 |
| AU 722425 | B2 | 20000803 | | |
| EP 925503 | A1 | 19990630 | EP 1997-939083 | 19970911 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1234118 | A | 19991103 | CN 1997-199097 | 19970911 |
| BR 9711753 | A | 20000118 | BR 1997-11753 | 19970911 |
| JP 2001505658 | T2 | 20010424 | JP 1998-513366 | 19970911 |
| PRIORITY APPLN. INFO.: | | | GB 1996-18934 A | 19960911 |
| | | | WO 1997-GB2440 W | 19970911 |

AB The diagnosis of diabetes based on the level or ratio of P- and A-type inositolphosphoglycans (IPGs) in a sample from a patient, and the use of P- and A-type IPGs or their antagonists in the treatment of diabetes, are disclosed. In particular, the invention provides treatment of IDDM or lean type II diabetes (NIDDM) with a mixt. of P- and A-type mediators, and treatment of obese type II diabetes (NIDDM) with a P-type mediator and/or an A-type antagonist.

L10 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:180889 CAPLUS
 DOCUMENT NUMBER: 128:240997
 TITLE: Cyclitol containing carbohydrates from human tissue which regulate glycogen metabolism and their use in pharmaceuticals
 INVENTOR(S): Rademacher, Thomas William; Caro, Hugo
 PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
 SOURCE: PCT Int. Appl., 64 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|------------------|--------------|
| WO 9811117 | A1 | 19980319 | WO 1997-GB2533 | 19970911 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| AU 9743101 | A1 | 19980402 | AU 1997-43101 | 19970911 |
| AU 713100 | B2 | 19991125 | | |
| EP 925304 | A1 | 19990630 | EP 1997-919168 | 19970911 |
| EP 925304 | B1 | 20000426 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 192160 | E | 20000515 | AT 1997-919168 | 19970911 |
| ES 2147988 | T3 | 20001001 | ES 1997-919168 | 19970911 |
| JP 2001500859 | T2 | 20010123 | JP 1998-513410 | 19970911 |
| US 6271204 | B1 | 20010807 | US 1999-254748 | 19990614 |
| PRIORITY APPLN. INFO.: | | | GB 1996-18929 A | 19960911 |
| | | | WO 1997-GB2533 W | 19970911 |

AB The application relates to the purifn. and characterization of a family of P-type inositolphosphoglycans (IPGs) from human liver and placenta. These substances are shown to have P-type biol. activity, e.g., activating pyruvate dehydrogenase (PDH) phosphatase. The characterization of the compds. demonstrates that they contain metal ions, in particular Mn²⁺ and/or Zn²⁺, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g., for the treatment of diabetes, and in screening for synthetic analogs.

L10 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:180785 CAPLUS
 DOCUMENT NUMBER: 128:226268
 TITLE: P-type inositolphosphoglycans and antagonists thereof in diagnosis and treatment of pre-eclampsia and diabetes
 INVENTOR(S): Rademacher, Thomas William; Mclean, Patricia
 PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Mclean, Patricia
 SOURCE: PCT Int. Appl., 63 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-----------------|--------------|
| WO 9810791 | A1 | 19980319 | WO 1997-GB2534 | 19970911 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| AU 9743102 | A1 | 19980402 | AU 1997-43102 | 19970911 |
| AU 715884 | B2 | 20000210 | | |
| EP 939651 | A1 | 19990908 | EP 1997-919169 | 19970911 |

EP 939651 B1 20000531
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI
 CN 1235556 A 19991117 CN 1997-199318 19970911
 BR 9711752 A 20000118 BR 1997-11752 19970911
 AT 193452 E 20000615 AT 1997-919169 19970911
 ES 2148967 T3 20001016 ES 1997-919169 19970911
 JP 2001501598 T2 20010206 JP 1998-513411 19970911
 PRIORITY APPLN. INFO.: GB 1996-18931 A 19960911
 WO 1997-GB2534 W 19970911

AB The invention relates to materials and methods for the diagnosis and treatment of pre-eclampsia, and more particularly to the role of P-type inositolphosphoglycans (IPGs) in the occurrence of pre-eclampsia. Methods of diagnosing pre-eclampsia by detg. the level of P-type IPGs and uses of antagonists of P-type IPGs in the treatment of pre-eclampsia are disclosed, together with a method for screening for P-type IPG antagonists.

L10 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
 ACCESSION NUMBER: 1998:500068 CAPLUS

DOCUMENT NUMBER: 129:286317
 TITLE: Induction of cell growth by insulin and insulin-like growth factor-I is associated with Jun expression in the otic vesicle

AUTHOR(S): Leon, Yolanda; Sanz, Carmen; Giraldez, Fernando;

CORPORATE SOURCE: Instituto de Investigaciones Biomedicas, Consejo Superior de Investigaciones Cientificas (CSIC), Madrid, 28029, Spain

SOURCE: Journal of Comparative Neurology (1998), 398 (3), 323-332

CODEN: JCNEAM; ISSN: 0021-9967

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The present report investigates the cellular mechanisms involved in the regulation of cell proliferation by insulin and insulin-like growth factor-I (IGF-I) in the developing inner ear of chick embryos. The results show that insulin and IGF-I stimulate cell proliferation in the otic vesicle. This effect is assocd. with the induction of the expression of the nuclear proto-oncogene c-jun. The temporal profile of Jun expression coincided with the proliferative period of growth of the otic vesicle. IGF-I promoted the hydrolysis of a membrane glycosyl-phosphatidylinositol, which was characterized as the endogenous precursor for inositol phosphoglycan (IPG). Both purified IPG and a synthetic analog, 6-O-(2-amino-2-deoxy-.alpha.-D-glucopyranosyl)-D-myo-inositol-1,2-cyclic phosphate (C3), were able to mimic the effects of IGF-I on Jun expression. Anti-IPG antibodies blocked the effects of IGF-I, which were rescued by the addn. of IPG or its analog. These results suggest that the sequence involving the hydrolysis of membrane glycolipids and the expression of c-jun and c-fos proto-oncogenes is part of the mechanism that activates cell division in response to insulin and IGF-I during early organogenesis of the avian inner ear. The implications of these observations for otic development and regeneration are briefly discussed.

L10 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER: 1997:188451 CAPLUS
 DOCUMENT NUMBER: 126:272579
 TITLE: Inositol-phosphoglycan inhibits calcium oscillations in hepatocytes by reducing calcium entry

AUTHOR(S): Sanchez-Bueno, Antonio; Greenwood, Mark R.; Varela-Nieto, Isabel; Marrero, Isabel; Gil, Beatriz; Mato, Jose M.; Cobbold, Peter H.

CORPORATE SOURCE: Dep. Human Anatomy & Cell Biology, Univ. Liverpool, Liverpool, UK

SOURCE: Cell Calcium (1997), 21(2), 125-133

CODEN: CECADV; ISSN: 0143-4160

PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Inositol-phosphoglycan (IPG) is a putative mediator of insulin action that has been shown to affect numerous biochem. processes. IPG, prep'd. from liver membranes, promptly inhibited phenylephrine- or vasopressin-induced [Ca²⁺]_i oscillations when perfused over Fura-2-dextran injected rat hepatocytes. An antibody to IPG suppressed the inhibitory effect of insulin on the [Ca²⁺]_i oscillations. Measurement of the rate of quench of cytoplasmic Fura-2 by extracellular Mn²⁺ showed that Ca²⁺ entry occurred continuously in the unstimulated cell and was not affected by phenylephrine or vasopressin. IPG, specifically, almost completely abolished the Mn²⁺ quench rate. Elevated extracellular [Ca²⁺] reversed the inhibitory effect of IPG on [Ca²⁺]_i oscillations. We conclude that IPG inhibits the hepatocyte Ca²⁺ oscillator by reducing the continuous Ca²⁺ influx that is required to sustain oscillations in [Ca²⁺]_i.

L10 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3

ACCESSION NUMBER: 2000:345870 CAPLUS
 Correction of: 1997:525491

DOCUMENT NUMBER: 132:320044
 Correction of: 127:232322

TITLE: HDL3 binds to glycosylphosphatidylinositol-anchored proteins to activate signalling pathways
 AUTHOR(S): Nasih-Sanderson, Francoise; Lestavel, Sophie; Nion, Stephane; Rouy, Didier; Denefle, Patrice; Fruchart, Jean-Charles; Clavey, V.; Delbart, Christiane

CORPORATE SOURCE: Institut Pasteur, Lille, 59019, Fr.
 SOURCE: Biochimica et Biophysica Acta (1997), 1358(1), 103-112

CODEN: BBACAQ; ISSN: 0006-3002

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Previous studies have indicated that in HepG2 cells HDL3-signaling involves glycosylphosphatidylinositol (GPI) anchored proteins. HDL3-binding to HepG2 cells was found to be enhanced by cellular preincubation with PI-PLC inhibitors and sensitive to a cellular preincubation with exogenous PI-PLC, suggesting that HDL3 binds directly on GPI-anchored proteins to initiate signaling. Moreover HDL3-binding was found to be partly inhibited by antibodies against the HDL-binding protein (AbHBP). HDL3, when binding to HepG2 cells, promoted the release in the culture medium of a 110 kDa protein that binds AbHBP, while a cellular preincubation with antibodies against the inositol-phosphoglycan

(IPG) moiety of GPI-anchor (AbIPG), used to block lipolytic cleavage of the GPI-anchor, inhibits HDL3-induced release of the 110 kDa protein in the culture medium. In [³H]-PC prelabeled HepG2 cells, AbHBP were found to stimulate PC-hydrolysis and DAG generation within 5 min as did HDL3 stimulation. Cellular preincubation with AbIPG was found to inhibit only the HDL3-signal and not the AbHBP-signal, while a prior cellular pretreatment with PI-PLC from *Bacillus cereus* was found to inhibit the HDL3-and AbHBP-signal. Moreover cellular preincubation with AbHBP for 1 h at 37.^{degree}C was found to inhibit HDL3-signaling pathways. Our results suggest that in HepG2 cells a 110 kDa protein, which could be HBP, can be anchored to the membrane via GPI, and can function in HDL3-signaling pathways as binding sites. Previous studies have indicated that in HepG2 cells HDL3-signaling involves glycosylphosphatidylinositol (GPI) anchored proteins. HDL3-binding to HepG2 cells was found to be enhanced by cellular preincubation with PI-PLC inhibitors and sensitive to a cellular preincubation with exogenous PI-PLC, suggesting that HDL3 binds directly on GPI-anchored proteins to initiate signaling. Moreover HDL3-binding was found to be partly inhibited by antibodies against the HDL-binding protein (AbHBP). HDL3, when binding to HepG2 cells, promoted the release in the culture medium of a 110 kDa protein that binds AbHBP, while a cellular preincubation with antibodies against the inositol-phosphoglycan (IPG) moiety of GPI-anchor (AbIPG), used to block lipolytic cleavage of the GPI-anchor, inhibits HDL3-induced release of the 110 kDa protein in the culture medium. In [³H]-PC prelabeled HepG2 cells, AbHBP were found to stimulate PC-hydrolysis and DAG generation within 5 min as did HDL3 stimulation. Cellular preincubation with AbIPG was found to inhibit only the HDL3-signal and not the AbHBP-signal, while a prior cellular pretreatment with PI-PLC from *Bacillus cereus* was found to inhibit the HDL3-and AbHBP-signal. Moreover cellular preincubation with AbHBP for 1 h at 37.^{degree}C was found to inhibit HDL3-signaling pathways. Our results suggest that in HepG2 cells a 110 kDa protein, which could be HBP, can be anchored to the membrane via GPI, and can function in HDL3-signaling pathways as binding sites.

L10 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
 ACCESSION NUMBER: 1997:256377 CAPLUS
 DOCUMENT NUMBER: 126:328530
 TITLE: HDL3-signaling in HepG2 cells involves glycosyl-phosphatidylinositol-anchored proteins
 AUTHOR(S): Nazih-Sanderson, Francoise; Pinchon, Gaelle; Nion, Stephane; Fruchart, Jean-Charles; Delbart, Christiane
 CORPORATE SOURCE: Unite INSERM 325, Institut Pasteur, 1 rue du Professeur Calmette BP 245-59019, Lille, Fr.
 SOURCE: Biochimica et Biophysica Acta (1997), 1346(1), 45-60
 CODEN: BBACAQ; ISSN: 0006-3002
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In [³H]phosphatidylcholine (PC) prelabeled HepG2 cells, HDL3 stimulates a biphasic increase in 1,2-diacylglycerol (DAG). The early phase is mediated in part by a phospholipase C which is inhibited by 10 .mu.M D 609, RHC-80267 or U-73122 and less by 100 .mu.M propranolol. A phospholipase D is more likely involved in the late phase, as the DAG peak lags behind phosphatidic acid rise and is blocked by 100 .mu.M propranolol. Cellular preincubation with 200 .mu.g/mL antibodies against the inositolphosphoglycan (IPG) moiety of the GPI-anchor (AbIPG) or depletion in GPI-anchored proteins by cellular pretreatment with 0.5 U/mL PI-PLC, 1 mM insulin and 2 HU/mL streptolysin-O, or depletion in membrane cholesterol content by filipin (5 .mu.g/mL), digitonin (5 .mu.g/mL) and cholesterol oxidase (0.5 U/mL) decreases the HDL3-signal, suggesting the involvement of lipolytic cleavage of GPI-anchored proteins. Inhibition of proteases by 1 mM leupeptin/PMSF improves the response time to HDL3, with a DAG peak at 2-3 min. In the presence of protease-inhibitors, HDL3 releases in the culture medium several proteins with a residual IPG that binds AbIPG after SDS-PAGE anal. and immunoblotting. HDL3-signaling pathways comprise tyrosine kinases, as preincubation with 100 .mu.g/mL genistein or tyrphostin inhibits the HDL3-signal. HDL3 activates PC hydrolysis through a multistep pathway involving the cleavage of GPI-anchored proteins.

L10 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
 ACCESSION NUMBER: 1995:716457 CAPLUS
 DOCUMENT NUMBER: 123:103494
 TITLE: Insulin-like growth factor-I regulates cell proliferation in the developing inner ear, activating glycosyl-phosphatidylinositol hydrolysis and fos expression
 AUTHOR(S): Leon, Yoland; Vazquez, Esther; Sanz, Carmen; Vega, Jose A.; Mato, Jose M.; Giraldez, Fernando; Represa, Juan; Varela-Nieto, Isabel
 CORPORATE SOURCE: Inst. Invest. Biomed., Cons. Super Invest. Cient., Madrid, 28029, Spain
 SOURCE: Endocrinology (1995), 136(8), 3494-503
 CODEN: ENDOAO; ISSN: 0013-7227
 PUBLISHER: Endocrine Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The role of insulin-like growth factors (IGF) was investigated during the early development of the inner ear. IGF-I stimulated growth of otic vesicles that were isolated and cultured in vitro. IGF-I induced DNA synthesis, increased cell no., and mitotic rate in a dose-dependent manner at concns. between 0.1-10 nM. IGF-I also induced growth but with a lower potency, whereas insulin had no effect. In the presence of IGF-I, otic vesicles developed from stage 18 to stage 21 in 24-h cultures, mimicking the normal mitotic pattern and morphogenesis in vivo. IGF-I also stimulated growth in the cochleo-vestibular ganglion. Binding of ¹²⁵I-IGF-I to specific receptors occurred with high affinity. An autoradiog. study of sections from otic vesicles showed radiolabeled IGF-I in the epithelium. Immunoreactivity to IGF-I was detected in the otic vesicle and in the cochleo-vestibular ganglion. Intracellular signaling mechanisms of IGF were explored by studying the turnover of glycosylated phosphatidylinositols and the expression of Fos oncogene. IGF-I rapidly increased Fos levels in cultured otic vesicles. Furthermore, antisense oligonucleotides complementary to c-fos were able to inhibit IGF-I-induced growth. Both IGF-I-induced cell proliferation and Fos expression were blocked by an antinositol phosphoglycan (.alpha.-IPG) antibody. This work suggests that IGF-I may be a candidate to regulate proliferative growth of the otic primordium during normal development and that this action requires the sequential modulation of glycosyl-phosphatidylinositol turnover and Fos expression.

L10 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6

ACCESSION NUMBER: 1995:727759 CAPLUS
DOCUMENT NUMBER: 123:133829
TITLE: Role of glycosyl-phosphatidylinositol hydrolysis as a mitogenic signal for epidermal growth factor
AUTHOR(S): Clemente, Rosa; Jones, David R.; Ochoa, Pilar; Romero, Guillermo; Mato, Jose M.; Varela-Nieto, Isabel
CORPORATE SOURCE: Consejo Superior de Investigaciones Cientificas (CSIC), Instituto de Investigaciones Biomedicas, Madrid, 28029, Spain
SOURCE: Cellular Signalling (1995), 7(4), 411-21
CODEN: CESIEY; ISSN: 0898-6568
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have investigated the role of the hydrolysis of glycosyl-phosphatidylinositol (GPI) as one of the signaling pathways elicited after interaction of epidermal growth factor (EGF) with its specific plasma membrane receptor (EGFR). Endogenous GPI was characterized in both NIH 3T3 mouse fibroblast cells and in EGFR-transfected NIH 3T3 cells (designated EGFR T17). GPI mols. isolated from both cell lines were identical and they incorporated radioactivity from both sugar and fatty acid substrates. Incubation of EGFR T17 cells with EGF, produced a rapid and transient hydrolysis of GPI. Max. hydrolysis occurred after a 1-min incubation with 50 nM EGF. No such effects of EGF were obsd. in the parental cell line. Both inositol phosphoglycan (IPG)- and EGF-induced cell proliferation was inhibited in the presence of an IPG-antibody to different extents. The relation between GPI hydrolysis and the activity of the EGFR was studied using the tyrosine kinase inhibitors tyrphostin (RG50864) and genistein. These agents were able to significantly inhibit EGF-mediated cell proliferation, EGF-dependent hydrolysis of GPI and EGF-regulated autophosphorylation of the EGFR. It is concluded that GPI hydrolysis is one of the earliest intracellular events generated in response to EGF.

L10 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:647461 CAPLUS
DOCUMENT NUMBER: 123:29944
TITLE: Intracellular mediators of insulin-like growth factor I during otic vesicle development
AUTHOR(S): Leon, Yolanda; Sanz, Carmen; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Investigaciones Biomedicas, Madrid, 28029, Spain
SOURCE: Biochemical Society Transactions (1995), 23(2), 185S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors examd. the participation of the glycosylphosphatidylinositol (GPI)/inositol phosphoglycan (IPG) signaling system in the mediation of the proliferative effects of IGF-I in the developing otic vesicle and its relationship with Fos oncprotein expression. IGF-I induced a fast and transient hydrolysis of GPI. The proliferative effects of IGF-I were coupled to GPI hydrolysis. The resulting IPG is a crucial step for the transduction of the mitogenic signal since anti-IPG antibodies decreased the effect on IP-I on otic vesicle growth in parallel with a decrease in Fos oncprotein expression.

L10 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:647450 CAPLUS
DOCUMENT NUMBER: 123:26347
TITLE: Signalling at the epidermal growth factor receptor: role of glycosylphosphatidylinositol hydrolysis
AUTHOR(S): Jones, David R.; Clemente, Rosa; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Investigaciones Biomedicas, Madrid, 28029, Spain
SOURCE: Biochemical Society Transactions (1995), 23(2), 174S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors investigated the involvement of glycosylphosphatidylinositol (GPI) hydrolysis during EGF-induced cell proliferation both in 3T3 cells and in 3T3 cells overexpressing the cloned human EGF receptor (EGFR T17 cells). The results showed that EGF modulated GPI turnover in an EGF receptor-dependent manner; EGF action was dose- and time-dependent; inositol phosphoglycan (IPG) specifically stimulated EGFR T17 cell proliferation; anti-IPG antibodies inhibited EGF-dependent cell proliferation; and tyrosine kinase inhibitors partially blocked GPI hydrolysis in parallel with the inhibition of both EGFR autophosphorylation and EGF-induced cell proliferation. proliferation. Thus, tyrosine kinase dependent-GPI hydrolysis may represent an early event in the transduction of the EGF signal in EGFR T17 cells.

L10 ANSWER 12 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
ACCESSION NUMBER: 93167402 EMBASE
DOCUMENT NUMBER: 1993167402
TITLE: IPG (inositolphosphate glycan) as a cellular signal for TGF-.beta.1 modulation of chondrocyte cell cycle.
AUTHOR: Vivien D.; Petitfrère E.; Martiny L.; Sartelet H.; Galéra P.; Haye B.; Pujol J.-P.
CORPORATE SOURCE: Lab. Biochimie du Tissu Conjonctif, CJF INSERM 91-06, CHU Cote de Nacre, 14033 Caen Cedex, France
SOURCE: Journal of Cellular Physiology, (1993) 155/3 (437-444).
ISSN: 0021-9541 CODEN: JCLLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The knowledge of transforming growth factor (TGF)-.beta. receptors has greatly progressed in recent years. TGF-.beta. receptors type I and II have been implicated in the modulation of cell proliferation, whereas type III (betaglycan) may act as a component presenting TGF-.beta. to its signaling receptors. In addition, four other proteins that bind TGF-.beta.1 or TGF-.beta.2 have been recently identified in some cell lines, three being anchored to the membrane through a glycosylphosphatidylinositol (GPI). Despite this knowledge, the molecular mechanism of signal transduction through the TGF-.beta. receptors remain an enigma. TGF-.beta. family does not signal via any of the classical pathways. As GPI anchors of membrane proteins have been implicated in the

transduction of some hormonal effects, we investigated the putative role of GPI in signaling the TGF-.beta. effects on the proliferation of rabbit articular chondrocytes (RAC). We previously showed that TGF-.beta.1 increased DNA replication rate of RAC, with a recruitment of cells in G2/M followed by a subsequent mitosis wave. Here, we find that the factor causes specific GPI hydrolysis, with correlated increase of inositolphosphate glycan (IPG). This effect was specifically inhibited by antibodies that bind TGF-.beta.1. Using [³H]-inositol labeling and Triton X-114 extraction, we demonstrate that a hydrophobic material from the membrane is cleaved by treatment of cell cultures with phosphatidylinositol specific phospholipase C (PI-PLC) or by exposure to TGF-.beta., supporting that a PI-anchored molecule gives rise to IPG by TGF-.beta.-induced hydrolysis. The biological relevance of this hydrolysis was demonstrated by the enhancing effect of purified IPG on the DNA synthesis rate, which mimicked the TGF-.beta. action. These results demonstrate that IPG could be an early messenger in the cellular signaling that mediates the effect of TGF-.beta. on RAC growth.

L10 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
 ACCESSION NUMBER: 1994:5158 CAPLUS
 DOCUMENT NUMBER: 120:5158
 TITLE: Brain-derived neurotrophic factor and neurotrophin-3 support the survival and neuritogenesis response of developing cochleovestibular ganglion neurons
 AUTHOR(S): Avila, Matias A.; Varela-nieto, Isabel; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Van de Water, Thomas R.; Represa, Juan
 CORPORATE SOURCE: Inst. Invest Biomed, Cons. Super. Invest. Cient., Madrid, 28029, Spain
 SOURCE: Developmental Biology (Orlando, FL, United States) (1993), 159(1), 266-75
 CODEN: DEBIAO; ISSN: 0012-1606
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The effects of brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) on the differentiation of avian cochleovestibular ganglion and their possible assocn. with the hydrolysis of glycosyl-phosphatidylinositol (GPI) were studied. BDNF and NT-3 (2 ng/mL) promoted neurite outgrowth in explants of both cochlear and vestibular ganglia. This effect on neuritogenesis was stage-dependent, reaching a max. at E7 for NT-3 and at E9 for BDNF. The magnitude of the response of the vestibular ganglion to BDNF was always smaller than that of the cochlear ganglion of an equiv. stage. BDNF and NT-3 stimulation of neuronal survival and neurite extension was also demonstrated in dissociated neuronal cell cultures. The effect was concn.-dependent with satn. of the response occurring at 4 ng/mL for BDNF and at 2 ng/mL for NT-3, the half-maximal effect occurring at 2 and 1 ng/mL, resp., for the most sensitive stages of the chick cochlear ganglion. Inositol phosphoglycan (IPG) did not mimic the effects of BDNF or NT-3 on neuronal survival and neurite outgrowth, nor was it able to potentiate their responses. Antibodies raised against IPG did not block the effects of these neurotrophins. The results suggest that BDNF and NT-3 may act in cooperation to establish the innervation pattern of the inner ear. Unlike their early proliferative effects, neurotrophic effects are uncoupled from the GPI/IPG signal transduction system.

L10 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:618227 CAPLUS
 DOCUMENT NUMBER: 119:218227
 TITLE: Brain-derived neurotrophic factor and neurotrophin-3 support the survival and neuritogenesis response of developing cochleovestibular ganglion neurons
 AUTHOR(S): Avila, Matias A.; Varela-Nieto, Isabel; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Van De Water, Thomas R.; Represa, Juan
 CORPORATE SOURCE: Inst. Invest. Biomed., Cons. Super. Invest. Cient., Madrid, 28029, Spain
 SOURCE: Developmental Biology (Orlando, FL, United States) (1993), 159(2), 266-75
 CODEN: DEBIAO; ISSN: 0012-1606
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The effects of brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) on the differentiation of avian cochleovestibular ganglion and their possible assocn. with the hydrolysis of glycosyl-phosphatidylinositol (GPI) were studied. BDNF and NT-3 (2 ng/mL) promoted neurite outgrowth in explants of both cochlear and vestibular ganglia. This effect on neuritogenesis was stage-dependent, reaching a max. at E7 for NT-3 and at E9 for BDNF. The magnitude of the response of the vestibular ganglion to BDNF was always smaller than that of the cochlear ganglion of an equiv. stage. BDNF and NT-3 stimulation of neuronal survival and neurite extension was also demonstrated in dissociated neuronal cell cultures. The effect was concn.-dependent with satn. of the response occurring at 4 ng/mL for BDNF and at 2 ng/mL for NT-3, the half-maximal effect occurring at 2 and 1 ng/mL, resp., for the most sensitive stages of the chick cochlear ganglion. Inositol phosphoglycan (IPG) did not mimic the effects of BDNF or NT-3 on neuronal survival and neurite outgrowth, nor was it able to potentiate their responses. Antibodies raised against IPG did not block the effects of these neurotrophins. The results suggest that BDNF and NT-3 may act in cooperation to establish the innervation pattern of the inner ear. Unlike their early proliferative effects, neurotrophic effects are uncoupled from the GPI/IPG signal transduction system.

L10 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
 ACCESSION NUMBER: 1994:5157 CAPLUS
 DOCUMENT NUMBER: 120:5157
 TITLE: Brain-derived neurotrophic factor and neurotrophin-3 induce cell proliferation in the cochleovestibular ganglion through a glycosyl-phosphatidylinositol signaling system
 AUTHOR(S): Represa, Juan; Avila, Matias A.; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Verela-Nieto, Isabel
 CORPORATE SOURCE: Fac. Med., Univ. Valladolid, Valladolid, 47005, Spain
 SOURCE: Developmental Biology (Orlando, FL, United States) (1993), 159(1), 257-65
 CODEN: DEBIAO; ISSN: 0012-1606
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The authors have investigated the role of a brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) in the regulation of cell proliferation in the early developing cochleovestibular ganglion (CVG).

Ganglia were isolated from 72-h chick embryos and cultured for 24 h. Both BDNF and NT-3 had a powerful mitogenic effect, at doses of 1-5 ng/mL, consistent with an involvement of the high-affinity receptor. Evidence for the participation of the glycosyl-phosphatidylinositol (GPI)/inositol phosphoglycan (IPG) signaling system in the mediation of proliferative effects of BDNF and NT-3 is presented. Both of these neurotrophins elicited a fast and transient hydrolysis of labeled GPI, approx. 60% in 30 s. The dose-response profile of GPI hydrolysis overlaps the neurotrophin-induced cell proliferation response profile. Anti-IPG antibodies were able to block the growth-promoting effects of BDNF and NT-3. Anti-IPG antibodies immunopptd. a CVG-endogenous IPG, induced upon BDNF treatment, which exhibited proliferative stimulating properties. Both BDNF and NT-3 are proposed as potential candidates for regulation of growth during CVG development, with this mitogenic effect being mediated by the GPI/IPG signaling system.

L10 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:618226 CAPLUS
DOCUMENT NUMBER: 119:218226
TITLE: Brain-derived neurotrophic factor and neurotrophin-3 induce cell proliferation in the cochleovestibular ganglion through a glycosyl-phosphatidylinositol signaling system
AUTHOR(S): Represa, Juan; Avila, Matias; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Varela-Nieto, Isabel
CORPORATE SOURCE: Fac. Med., Univ. Valladolid, Valladolid, 47005, Spain
SOURCE: Developmental Biology (Orlando, FL, United States) (1993), 159(2), 257-65
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have investigated the role of brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) in the regulation of cell proliferation in the early developing cochleovestibular ganglion (CVG). Ganglia were isolated from 72-h chick embryos and cultured for 24 h. Both BDNF and NT-3 had a powerful mitogenic effect, at doses of 1-5 ng/mL, consistent with an involvement of the high-affinity receptor. Evidence for the participation of the glycosyl-phosphatidylinositol (GPI)/inositol phosphoglycan (IPG) signaling system in the mediation of proliferative effects of BDNF and NT-3 is presented. Both of these neurotrophins elicited a fast and transient hydrolysis of labeled GPI, approx. 60% in 30 s. The dose-response profile of GPI hydrolysis overlaps the neurotrophin-induced cell proliferation response profile. Anti-IPG antibodies were able to block the growth-promoting effects of BDNF and NT-3. Anti-IPG antibodies immunopptd. a CVG-endogenous IPG, induced upon BDNF treatment, which exhibited proliferative stimulating properties. Both BDNF and NT-3 are proposed as potential candidates for regulation of growth during CVG development, with this mitogenic effect being mediated by the GPI/IPG signaling system.

L10 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:1423 CAPLUS
DOCUMENT NUMBER: 120:1423
TITLE: Glycosyl-phosphatidylinositol: Role in neurotrophic factors signalling
AUTHOR(S): Avila, Matias A.; Leon, Yolanda; Gil, Beatriz; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Invest. Biomed., Cons. Super. Invest. Cient., Madrid, 28029, Spain
SOURCE: NATO ASI Series, Series A: Life Sciences (1993), 246 (New Developments in Lipid-Protein Interactions and Receptors Function), 103-13
CODEN: NALSDJ; ISSN: 0258-1213
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study provides further support for the involvement of the glycosyl-phosphatidylinositol/inositol-phosphoglycan (GPI/IPG) pathway in transducing the mitogenic effects of NGF on the early developing inner ear by showing: (1) the presence of endogenous GPI and IPG, the latter with strong mitogenic activity, (2) the ability of NGF to stimulate GPI hydrolysis in parallel with its biol. activity, (3) the ability of anti-IPG antibodies to block the biol. effects on NGF.

L10 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1992:252962 CAPLUS
DOCUMENT NUMBER: 116:252962
TITLE: Role of the glycosylphosphatidylinositol/inositol phosphoglycan system in human fibroblast proliferation
AUTHOR(S): Vasta, Valeria; Bruni, Paola; Clemente, Rosa; Vannini, Fabio; Ochoa, Pilar; Romero, Guillermo; Farnararo, Marta; Varela-Nieto, Isabel
CORPORATE SOURCE: Dip. Sci. Biochim., Univ. Firenze, Florence, 50134, Italy
SOURCE: Experimental Cell Research (1992), 200(2), 439-43
CODEN: ECREAL; ISSN: 0014-4827
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The involvement of the glycosylphosphatidylinositol/inositol phosphoglycan (gly-PtdIns/IPG) system in the stimulation of macromol. syntheses in human fibroblasts has been investigated. The study demonstrates that an insulin-sensitive gly-PtdIns/IPG system is present in human fibroblasts, that IPG can significantly stimulate DNA, RNA, and protein synthesis, and that the action of insulin on DNA synthesis as well as that of IPG can be significantly reduced by a specific anti-IPG antibody. These results strongly support the hypothesis that the gly-PtdIns/IPG system is involved in the signal transduction pathway leading to the stimulation of cell proliferation.

L10 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:410418 BIOSIS
DOCUMENT NUMBER: BA94:73618
TITLE: IMMOBILIZED PH GRADIENT ISOELECTRIC FOCUSING AND IMMUNOBLOTTING FOR INVESTIGATIONS OF ANTI-BORRELIA-BURGDORFERI IGG ANTIBODIES.
AUTHOR(S): CRUZ M; SIDEN A
CORPORATE SOURCE: DEP. NEUROL., HUDDINGE UNIV. HOSP., S-141 86 HUDDINGE, SWED.
SOURCE: ELECTROPHORESIS, (1992) 13 (4), 229-234.
CODEN: ELCTDN. ISSN: 0173-0835.
FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Anti-Borrelia burgdorferi immunoglobulin G (IgG) responses in cerebrospinal fluid, serum, and joint fluid from Lyme disease patients were investigated by immobilized pH gradient (IPG) isoelectric focussing (IEF) in pH 4-10 and pH 4-7 gels. After focusing, the anti-B. burgdorferi antibodies were blotted by affinity-driven transfer to antigen-coated polyvinylidene difluoride membranes (immunoblot) and the IgG antibodies were immunoenzymatically stained. IPG-IEF gels gave an excellent resolution of IgG and the immunoblot proved advantageous for the detection of anti-B. burgdorferi IgG antibodies. These antibodies, as judged from the electromigration characteristics, were found to contain oligoclonal as well as polyclonal subpopulations. This latter group included IgG antibodies that were inadequately resolved when separated by conventional carrier ampholyte IEF.

L10 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11

ACCESSION NUMBER: 1991:599685 CAPLUS

DOCUMENT NUMBER: 115:199685

TITLE: Glycosyl-phosphatidylinositol/inositol phosphoglycan: a signaling system for the low-affinity nerve growth factor receptor

AUTHOR(S): Represa, Juan; Avila, Matias A.; Miner, Cristina; Giraldez, Fernando; Romero, Guillermo; Clemente, Rosa; Mato, Jose M.; Varela-Nieto, Isabel

CORPORATE SOURCE: Fac. Med., Univ. Valladolid, Valladolid, 47005, Spain
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1991), 88(18), 8016-19

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nerve growth factor (NGF) exerts a variety of actions during embryonic development. At the early stages of inner ear development, NGF stimulates cell proliferation, an effect mediated through low-affinity receptors. The possibility that the glycosyl-phosphatidylinositol/inositol phosphoglycan (glycosyl-PtdIns/IPG) system is involved in transmitting this NGF signal was studied. Endogenous glycosyl-PtdIns was characterized in exts. of cochleovestibular ganglia (CVGs) that incorporated [³H]glucosamine, [³H]galactose, [³H]myristic acid, and [³H]palmitic acid. Incubation of CVG with NGF produced a rapid and transient hydrolysis of glycosyl-PtdIns. Hydrolysis was complete at 100 ng/mL, and the half-maximal effect occurred at 25 ng/mL, overlapping with the concn. dependence of the mitogenic effect of NGF. An IPG was isolated from embryonic exts. It had biol. effects similar to those reported for the insulin-induced IPG in other tissues. It exerted a powerful mitogenic effect on CVG, comparable to that of NGF. Both the IPG- and NGF-induced cell proliferation were blocked by anti-IPG antibodies that recognized the endogenous IPG on a silica plate immunoassay. These results show that CVG possesses a fully active glycosyl-PtdIns/IPG signal transduction system and that the proliferative effects assocd. with NGF binding to low-affinity receptors require IPG generation.

L10 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12

ACCESSION NUMBER: 1991:22112 CAPLUS

DOCUMENT NUMBER: 114:22112

TITLE: Shifts of isoelectric points between cellular and secreted antibodies as revealed by isoelectric focusing and immobilized pH gradients

AUTHOR(S): Wenisch, Elisabeth; Reiter, Susanne; Hinger, Susanne; Steindl, Franz; Tauer, Christa; Jungbauer, Alois; Katinger, Hermann; Righetti, Pier Giorgio

CORPORATE SOURCE: Inst. Appl. Microbiol., Univ. Agric. For., Vienna, Austria

SOURCE: Electrophoresis (1990), 11(11), 966-9

CODEN: ELCTDN; ISSN: 0173-0835

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Charge microheterogeneity of monoclonal antibodies, as revealed by isoelec. focusing in carrier ampholytes, has been known for a long time. Here in the case of monoclonals against the gp41 of the HIV-1 virus, this heterogeneity is already present within the cell sap of hybridoma cells during antibody synthesis. When the monoclonals are secreted extracellularly, the same pI spectrum is maintained, but there is a marked redistribution of the relative isoform abundance towards the lower pI components. This suggests *in vivo* processing of such forms, possibly via glycosylation or deamidation. The secreted antibodies are also analyzed by immobilized pH gradients (IPG), where they demonstrate an even more extensive heterogeneity, due to the marked increment in resolving power. Single bands are purified by preparative IPGs in a multicompartment electrolyzer and are shown to be stable with time. Thus, artifactual heterogeneity produced by the focusing technique is completely excluded and cellular processing is clearly established.

L10 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13

ACCESSION NUMBER: 1990:135487 CAPLUS

DOCUMENT NUMBER: 112:135487

TITLE: Analytical isoelectric focusing with immobilized pH gradients of human apolipoprotein E from very low density lipoproteins and total plasma

AUTHOR(S): Maily, France; Davignon, Jean; Nestruck, A. Christine Hyperlipidemia Atherosclerosis Res. Group, Inst. Rech. Clin. Montreal, Montreal, PQ, H2W 1R7, Can.

SOURCE: J. Lipid Res. (1990), 31(1), 149-55

CODEN: JLPRAW; ISSN: 0022-2275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method for anal. isoelec. focusing (IEF) of apolipoprotein E (apoE) in immobilized pH gradients (IPG) and immunodetection of the sepd. isoforms has been developed for use with either very-low-d. lipoproteins (VLDL) or whole plasma. Both VLDL and plasma were sequentially delipidated with 1,4-dioxane, acetone-ethanol, and ether. Neuraminidase treatment preceded the delipidation when required. Using preformed plates, pH 5.0-6.0 (LKB, Bromma) after rehydration with 6M urea and dextran T-10, the IPG focusing pattern of the common isoforms (E2, E3, E4) was found to be equiv. to conventional IEF with the added resoln. of the E4 disialo form. The use of self-poured narrower gradients permitted the further resoln. of the E4 monosialo form, a previously unrecognized heterogeneity of the E2, E3, and E4 monosialo isoforms and differentiation of the apoE^{2**} mutant; all of these forms comigrate with the common isoproteins in conventional IEF. Finally, the conditions for IPG of whole plasma using apoE monoclonal antibodies and enzyme-conjugated anti-mouse IgG for detection were established. Thus, IPG focusing is shown to be a powerful

method for resoln. of the apoE sialoforms and apoE mutant forms. The method has important implications in accurate and diagnostic phenotyping. Moreover, it is a convenient method for phenotyping which requires only very small vols. of plasma.

L10 ANSWER 23 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 14

ACCESSION NUMBER: 87059320 EMBASE

DOCUMENT NUMBER: 1987059320

TITLE: A double-blind placebo-controlled trial of polymerized whole grass administered in an accelerated dosage schedule for immunotherapy of grass pollinosis.

AUTHOR: Grammer L.C.; Shaughnessy M.A.; Finkle S.M.; et al.

CORPORATE SOURCE: Section of Allergy-Immunology, Department of Medicine, Northwestern University Medical School, Chicago, IL 60611, United States

SOURCE: Journal of Allergy and Clinical Immunology, (1986) 78/6 (1180-1184).

CODEN: JACIBY

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index

LANGUAGE: English

AB Forty-four patients were entered into a study of the efficacy and safety of individually polymerized grass (IPG) immunotherapy with an accelerated dosage schedule. Patients were paired on the basis of cutaneous end point titrations to timothy, orchard, and Bermuda grass-pollen extracts. In a double-blind manner, one patient in each pair was treated in nine weekly visits with 13 injections that totaled 24,000 PNU of each grass to which the patient had cutaneous reactivity. The other patient in each pair received caramelized glucose histamine placebo. Symptom and medication score sheets were completed by 33 patients each day of the grass season. Blocking antibody rose significantly in the IPG-treated group but was unchanged in the placebo-treated group. By Wilcoxon paired signed-rank test, the symptom medication scores in the IPG-treated group were significantly lower than those in the placebo-treated group. There were no systemic reactions and no clinically significant changes in routine laboratory tests in either group. In summation, this study demonstrates the safety, immunogenicity, and efficacy of IPG therapy in an accelerated dosage schedule for treatment of grass pollinosis.

L10 ANSWER 24 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 15

ACCESSION NUMBER: 84030958 EMBASE

DOCUMENT NUMBER: 1984030958

TITLE: A double-blind histamine placebo-controlled trial of polymerized whole grass for immunotherapy of grass allergy.

AUTHOR: Grammer L.C.; Shaughnessy M.A.; Suszko I.M.; et al.

CORPORATE SOURCE: Section of Allergy-Immunology, Department of Medicine, Northwestern University Medical School, Chicago, IL 60611, United States

SOURCE: Journal of Allergy and Clinical Immunology, (1983) 72/5 I (448-453).

CODEN: JACIBY

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 038 Adverse Reactions Titles

037 Drug Literature Index

026 Immunology, Serology and Transplantation

015 Chest Diseases, Thoracic Surgery and Tuberculosis

030 Pharmacology

LANGUAGE: English

AB Twenty-six patients were recruited for a study of the safety and efficacy of immunotherapy with IPG. They were randomly assigned to two groups based on skin test titrations to grass allergens. One group was treated in a double-blind fashion before the 1982 grass season with 12 weekly injections totaling approximately 48,000 PNU, and the other group was treated with 12 weekly injections of caramelized glucose histamine placebo. Daily symptom and medication score sheets were completed by all patients each day of the grass season. Blocking antibody rose ninefold in the IPG group ($p < 0.007$) but was unchanged in the placebo group. There was no significant change in IgE against rye grass group I in either the IPG or the placebo group. Symptom-score mean in the IPG group was 217 \pm 71 (S.E.M.), statistically lower ($p < 0.02$) than the mean in the placebo group 496 \pm 117 (S.E.M.). There were no systemic reactions and only minor local reactions. There was no change in routine laboratory tests in either group. Although two prior studies with grass allergen immunotherapy reported efficacy, these studies did not use symptom-score analysis. This is the first double-blind, histamine placebo-controlled study of grass immunotherapy that demonstrates efficacy by symptom-score index evaluation. IPG is a safe, clinically effective, and potentially cost-effective therapy for grass pollinosis.

L10 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1978:164188 CAPLUS

DOCUMENT NUMBER: 88:164188

TITLE: Pharmacological studies on an iron-poly(sorbitol-gluconic acid) complex for parenteral treatment of iron deficiency anemia

AUTHOR(S): Eriksson, Hans; Svärd, Per Olov

CORPORATE SOURCE: Res. Dev. Lab., Astra Lakemedel AB, Sodertalje, Swed. Scand. J. Haematol., Suppl. (1977), 32,

38-49

CODEN: SJHSBD; ISSN: 0080-6722

DOCUMENT TYPE: Journal

LANGUAGE: English

AB I.v. injection of the iron-poly(sorbitol-gluconic acid) complex (IPSG) to cats caused a transient decrease in mean arterial blood pressure and a temporary increase in central venous pressure, heart rate and femoral blood flow at large doses (cumulative doses up to 744 mg/kg). Tachyphylaxis developed upon repeated administration. A temporary redn. in the magnitude of the blood pressure responses to noradrenaline and isoprenaline was obtained after large doses of IPSG. The blood pressure effects of acetylcholine, histamine and bilateral carotid occlusion were not affected. No definite effects were seen on the EKGs. The transient cardiovascular effects were interpreted as being due to the presence of small amts. of Fe²⁺ in the prepn. IPSG did not affect blood coagulation or platelet aggregation. Immunogenicity studies in rabbits and antibody analyses of sera from patients treated with IPSG failed to demonstrate any effect of IPSG on the immune system.

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(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
L4 1 S L3 AND GPI-PLD
L5 1504 S (IPG OR (INOSITOLPHOSPHOGLYCANS))
L6 4 S L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
L7 3 DUP REM L6 (1 DUPLICATE REMOVED)
L8 80 S L5 (1ON) ANTIBOD?
L9 51 S L8 AND PD<19980327
L10 25 DUP REM L9 (26 DUPLICATES REMOVED)

=> s (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))\

MISSING OPERATOR INOSITOL)\
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))
L11 9525 (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))

=> s (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) antibod?
L12 122 (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) ANTIBOD?

=> s l12 and PD<19980327
'19980327' NOT A VALID FIELD CODE

3 FILES SEARCHED...
L13 67 L12 AND PD<19980327

=> dup rem l13
PROCESSING COMPLETED FOR L13
L14 42 DUP REM L13 (25 DUPLICATES REMOVED)

=> s l14 (1ON) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L59 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L61 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L63 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L65 (10A) ADMINIST?'
L15 0 L14 (1ON) ADMINIST?

=> s l14 (P) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L70 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L72 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L74 (P) ADMINIST?'
L16 0 L14 (P) ADMINIST?

=> dis l14 1-42 ibib abs

L14 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180888 CAPLUS
DOCUMENT NUMBER: 128:242350
TITLE: A type A glycosylphosphatidylinositol second messenger
from human tissue involve in regulation of lipogenesis
INVENTOR(S): Rademacher, Thomas William; Caro, Hugo
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William;
Caro, Hugo
SOURCE: PCT Int. Appl., 62 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9811116 | A1 | 19980319 | WO 1997-GB2444 | 19970911 <- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TU, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, PR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9741307 | A1 | 19980402 | AU 1997-41307 | 19970911 |
| AU 713103 | B2 | 19991125 | | |
| EP 925305 | A1 | 19990630 | EP 1997-939087 | 19970911 |
| EP 925305 | B1 | 20000426 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI | | | | |
| AT 192161 | E | 20000515 | AT 1997-939087 | 19970911 |
| ES 2147996 | T3 | 20001001 | ES 1997-939087 | 19970911 |
| JP 2001504450 | T2 | 20010403 | JP 1998-513368 | 19970911 |
| US 6303580 | B1 | 20011016 | US 1999-254797 | 19990604 |
| US 2001039027 | A1 | 20011108 | US 2001-775856 | 20010201 |

PRIORITY APPLN. INFO.: GB 1996-18930 A 19960911
WO 1997-GB2444 W 19970911
US 1999-254797 A3 19990604

AB A family of A-type inositolphosphoglycans (IPGs) from human liver and
placenta that appear to play a role in the regulation of lipogenesis are
identified and characterized. These substances have the biol. activity
assocd. with A-type IPG fractions, namely regulating lipogenic activity
and inhibiting cAMP dependent protein kinase. The characterization of the
compd's. demonstrates that they contain metal ions, in particular Zn²⁺, and
optionally phosphate. The compds. and their antagonists have uses as
pharmaceuticals, e.g. for the treatment of diabetes, and in screening for
synthetic analogs.

L14 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 1998:645582 CAPLUS
DOCUMENT NUMBER: 130:3032
TITLE: Antibody crosslinking of the
glycosylphosphatidylinositol-linked protein

AUTHOR(S): Murray, Elizabeth W.; Robbins, Stephen M.
CORPORATE SOURCE: Cancer Biology and Immunology Research Groups,
Departments of Oncology and Biochemistry and Molecular
Biology, University of Calgary, Calgary, AB, T2N 4N1,
Can.

SOURCE: Journal of Biological Chemistry (1998),
273 (39), 25279-25284
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CD59 is a glycosylphosphatidylinositol-anchored cell surface glycoprotein involved in protecting cells from host-mediated complement attack. Studies have shown that antibody crosslinking of CD59 induces a series of intracellular signaling events including the activation of protein-tyrosine kinases (PTK). To further characterize these events, antibodies and complement 8, one of the natural ligands of CD59, were used to activate CD59. Antibody-induced crosslinking of CD59 on the surface of THP-1 and U937 hematopoietic cell lines as well as exposure to complement 8 induces a rapid increase in the tyrosine phosphorylation of several proteins within the cell. Consistent with an early role for the Src family PTKs in these signaling events, we found that transient activation of Hck- and CD59-mediated signaling was abrogated in the presence of the Src family PTK-selective inhibitor PP1. Although the mol. mechanism by which CD59 communicates to Hck is unknown, cellular fractionation studies indicated that both CD59 and Hck are compartmentalized in plasma membrane microdomains. We also detected tyrosine phosphorylation of the adaptor proteins p120cbl and Shc, and the cytoplasmic nonreceptor tyrosine kinase Syk. The identification of CD59-mediated signaling events may help explain why paroxysmal nocturnal hemoglobinuria patients, who are deficient in glycosylphosphatidylinositol-linked proteins including CD59, are susceptible to proliferative disorders.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:130801 CAPLUS
DOCUMENT NUMBER: 128:256338

TITLE: Cell activation mediated by glycosylphosphatidylinositol-anchored or transmembrane forms of CD14
AUTHOR(S): Pugin, J.; Kravchenko, V. V.; Lee, J. -D.; Kline, L.; Ulevitch, R. J.; Tobias, P. S.
CORPORATE SOURCE: Division of Medical Intensive Care, University Hospital, Geneva, 1211/14, Switz.

SOURCE: Infection and Immunity (1998), 66(3), 1174-1180

CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal
LANGUAGE: English

AB CD14 is a glycosylphosphatidylinositol (GPI)-anchored membrane glycoprotein which functions as a receptor on myeloid cells for ligands derived from microbial pathogens such as lipopolysaccharide (LPS). We have studied the importance of the GPI tail of CD14 in signaling with the promonocytic cell line THP-1 expressing recombinant CD14 in a GPI-anchored form (THP1-wtCD14 cells) or in a transmembrane form (THP1-tmCD14). We found that, like other GPI-anchored mol., GPI-anchored CD14 was recovered mainly from a Triton X-100-insol. fraction, whereas transmembrane CD14 was fully sol. in Triton X-100. LPS induced cell activation of THP1-wtCD14 and of THP1-tmCD14 (protein tyrosine kinase phosphorylation, NF-kappa.B activation, and cytokine prodn.) in a very similar manner. However, anti-CD14 antibody-induced crosslinking caused a rapid calcium mobilization signal only in GPI-anchored CD14 cells. Studies with pharmacol. inhibitors of intracellular signaling events implicate phospholipase C and protein tyrosine kinases in the genesis of this antibody-induced calcium signal. Our results suggest that GPI anchoring and CD14 targeting to glycolipid-rich membrane microdomains are not required for LPS-mediated myeloid cell activation. GPI anchoring may however be important for other signaling functions, such as those events reflected by antibody crosslinking.

L14 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:583862 CAPLUS
DOCUMENT NUMBER: 129:301394

TITLE: The glycosylphosphatidylinositol-anchored form and the transmembrane form of CD58 are released from the cell surface upon antibody binding

AUTHOR(S): Itzhaky, Dganit; Raz, Nava; Hollander, Nurit
CORPORATE SOURCE: Department Human Microbiology, Sackler School
Medicine, Tel-Aviv University, Tel-Aviv, 69978, Israel
SOURCE: Cellular Immunology (1998), 187(2), 151-157

CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The adhesion mol. CD58 is expressed on the cell surface in both a transmembrane form and a glycosylphosphatidylinositol (GPI)-anchored form. Here the authors report that CD58 is released from JY cells following crosslinking by immobilized anti-CD58 monoclonal antibodies. Antibodies to other cell surface proteins, as well as PMA and LPS, did not trigger CD58 release. The release resulted from membrane cleavage, since biotin-labeled CD58 was released from biotinylated cells, and down-modulation of CD58 surface expression accompanied accumulation of sol. CD58 in culture media. The authors have previously reported the isolation of JY variant cells, which lack expression of GPI-anchored proteins and thus express only the transmembrane form of CD58. Here they show that these variant cells release CD58 upon crosslinking, indicating that the transmembrane isoform is released, probably by proteolysis. Antibodies directed to the cytoplasmic domain of CD58, in contrast to antibodies against an extracellular epitope of CD58, did not react with released CD58, supporting a membrane cleavage mechanism. It is also shown that CD58, released from [³H]ethanolamine-labeled JY cells, contained ethanolamine. Thus, the GPI-anchored CD58 can be released in parallel to the transmembrane isoform and this release does not result from proteolytic cleavage, since cleavage by a protease would have removed the ethanolamine. Apparently, the 2 isoforms of CD58 are released upon antibody binding and their release is mediated by distinct mechanisms.

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REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:34080 CAPLUS
 DOCUMENT NUMBER: 126:55943
 TITLE: cysteine-rich glycosylphosphatidylinositol-anchored (CRG) protein gene marker for squamous cell carcinoma and bladder carcinoma as well as methods for diagnosis and treatment of these carcinomas
 INVENTOR(S): Brakenhoff, Rudolf Henrikus; Van Dongen, Augustina Antonius Maria Sylvester
 PATENT ASSIGNEE(S): Centocor B.V.; Neth.; Brakenhoff, Rudolf, Henrikus; Van Dongen, Augustina, Antonius, Maria, Sylvester
 SOURCE: PCT Int. Appl., 79 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-------------|
| WO 9635808 | A1 | 19961114 | WO 1995-NL168 | 19950510 -- |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9523758 | A1 | 19961129 | AU 1995-23758 | 19950510 -- |
| EP 028852 | A1 | 19980318 | EP 1995-916864 | 19950510 -- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| PRIORITY APPLN. INFO.: WO 1995-NL168 | | | | 19950510 |
| AB The subject invention lies in the field of malignant diseases. More specifically the invention lies in the field of squamous cell carcinoma and bladder carcinoma. The invention covers diagnosis and treatment of such forms of carcinoma. In particular the invention includes the detection of the presence and treatment of minimal residual disease, micrometastases or dissemination of such carcinoma types using nucleic acid hybridization or monoclonal antibody probes. The invention also includes gene therapy or vaccine development for treatment of carcinomas using cysteine-rich glycosylphosphatidylinositol-anchored protein (CRG protein) gene and expression vector constructs. CRG protein cDNA sequence is included, as well as characterization of CRG protein as the monoclonal antibody B48 antigen. | | | | |

L14 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
 ACCESSION NUMBER: 1996:355169 CAPLUS
 TITLE: The use of monoclonal antibodies and flow cytometry in the diagnosis of paroxysmal nocturnal hemoglobinuria
 AUTHOR(S): Hall, Sharon E.; Rosse, Wendell F.
 CORPORATE SOURCE: Department of Medicine, Duke University Medical Center, Durham, NC, 27710, USA
 SOURCE: Blood (1996), 87(12), 5332-5340
 DOCUMENT TYPE: CODEN: BLOOAW; ISSN: 0006-4971
 LANGUAGE: Journal English
 AB We have characterized the erythrocytes, granulocytes, and platelets of 54 patients with paroxysmal nocturnal hemoglobinuria (PNH) with antibodies to glycosylphosphatidylinositol-anchored proteins (anti-CD55, anti-CD59, and anti-CD16) and flow cytometry to establish the usefulness of this technique in the diagnosis of this disorder. All patients demonstrated either completely (PNH III) or partially (PNH II) deficient red cells and granulocytes. Anti-CD59 best demonstrated PNH II red cells, which were present in 50% of the patients. The proportion of abnormal granulocytes was usually greater than the proportion of abnormal red cells; 37% of the patients had >80% abnormal granulocytes. Anti-CD55 did not delineate the erythrocyte populations as well as did anti-CD59. Either anti-CD55 or anti-CD59 could be used equally well to analyze granulocytes; anti-CD16 did not demonstrate cells of partial deficiency. Platelets could not be used for detailed analysis as the normal and abnormal populations were not well distinguished. Flow cytometry of erythrocytes using anti-CD59 or of granulocytes using either anti-CD55 or anti-CD59 provides the most accurate technique for the diagnosis of paroxysmal nocturnal hemoglobinuria; it is clearly more specific, more quantitative, and more sensitive than the tests for PNH that depend upon hemolysis by complement (the acidified serum lysis [Ham] test, the sucrose lysis test, and the complement lysis sensitivity [CLS] test).

L14 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:123084 CAPLUS
 DOCUMENT NUMBER: 124:172196
 TITLE: Glycosylphosphatidylinositol toxin of Plasmodium induces nitric oxide synthase expression in macrophages and vascular endothelial cells by a protein tyrosine kinase-dependent and protein kinase C-dependent signaling pathway
 AUTHOR(S): Tachado, Souvenir D.; Gerold, Peter; McConville, Malcolm J.; Baldwin, Tracey; Quilici, Denis; Schwarz, Ralph T.; Schofield, Louis
 CORPORATE SOURCE: Immunoparasitology Unit, Royal Melbourne Hosp., Victoria, 3050, Australia
 SOURCE: Journal of Immunology (1996), 156(5), 1897-907
 DOCUMENT TYPE: CODEN: JOIMA3; ISSN: 0022-1767
 PUBLISHER: American Association of Immunologists
 LANGUAGE: English
 AB In this study, the authors demonstrate that glycosylphosphatidylinositol (GPI) is a major toxin of Plasmodium falciparum origin responsible for nitric oxide (NO) production in host cells. Purified malarial GPI is sufficient to induce NO release in a time- and dose-dependent manner in macrophages and vascular endothelial cells, and regulates inducible NO synthase expression in macrophages. GPI-induced NO production was blocked by the NO synthase-specific inhibitor L-N-monomethylarginine. GPI also synergizes with IFN- γ , in regulating NO production. The structurally related mols. dipalmitoylphosphatidylinositol and 1M4 glycoinositolphospholipid from Leishmania mexicana had no such activity, and the latter antagonized IFN- γ -induced NO output. GPI activates macrophages by initiating an early onset tyrosine kinase-mediated signaling process, similar to that induced by total parasite exts. The tyrosine kinase antagonists tyrphostin and genistein inhibited the release

of NO by parasite exts. and by GPI, alone or in combination with IPN-.gamma., demonstrating the involvement of one or more tyrosine kinases in the signaling cascade. GPI-induced NO release was also blocked by the protein kinase C inhibitor calphostin C, demonstrating a role for protein kinase C in GPI-mediated cell signalling, and by pyrrolidine dithiocarbamate, indicating the involvement of the NF-.kappa.B/c-rel family of transcription factors in cell activation. A neutralizing mAb to malarial GPI inhibited NO prodn. induced by GPI and total malarial parasite exts. in human vascular endothelial cells and murine macrophages, indicating that GPI is a necessary agent of parasite origin in parasite-induced NO output. Thus, in contrast to dipalmitoylphosphatidylinositol and glycoinositolphospholipids of Leishmania, malarial GPI initiates a protein tyrosine kinase- and protein kinase C-mediated signal transduction pathway, regulating inducible NO synthase expression with the participation of NF-.kappa.B/c-rel, which leads to macrophage and vascular endothelial cell activation and downstream prodn. of NO. These events may play a role in the etiol. of severe malaria.

L14 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
 ACCESSION NUMBER: 1996:363203 CAPLUS
 DOCUMENT NUMBER: 125:54187
 TITLE: mCD24 expression in the developing mouse brain and in zones of secondary neurogenesis in the adult
 AUTHOR(S): Calacra, V.; Chazal, G.; Nielsen, P. J.; Rougon, G.; Moreau, H.
 CORPORATE SOURCE: CNRS, Univ. Aix-Marseille II, Marseille, Fr.
 SOURCE: Neuroscience (Oxford) (1996), 73(2), 581-594
 CODEN: NRSCDN; ISSN: 0306-4522
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Interactions mediated by cell surface glycoproteins are considered to be crucial during the formation of the nervous system. Using a monoclonal antibody directed to mCD24, a glycosylphosphatidylinositol-anchored membrane glycoprotein, we have mapped its distribution throughout the mouse cerebral cortex during development and in young adult. Before birth, mCD24 immunoreactivity was obsd. in the intermediate zone, the cortical plate and the marginal zone, whereas the ventricular zones were immunoneg. After birth, mCD24 expression declined rapidly in the cortex, except in the corpus callosum (and other commissures in the brain) where immunoreactivity was still found until P20. Furthermore, mCD24 expression was maintained in young adults (until P60, at least) in zones of secondary neurogenesis, such as the granule cells of the dentate gyrus, the subventricular zone lining the anterior part of the lateral ventricles and a zone of cells extending between the striatum and the corpus callosum to the center of the olfactory bulb. In this area mCD24 and polysialic acid neural cell adhesion mol. stainings were superimposed, and this corresponded to the pathway of migration of the olfactory immature neurons (subependymal layer). A layer of ciliated ependymal cells, lining all the ventricular walls, was also immunoreactive for mCD24. Thus, except for these epithelial-like cells, mCD24 was essentially found assocd. with differentiating postmitotic neurons. Its spatiotemporal expression, both during development and in the adult, is compatible with a role for this glycoprotein in cell surface recognition and in signalling events occurring during neuronal migration and axonal growth.

L14 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:165185 CAPLUS
 DOCUMENT NUMBER: 124:229899
 TITLE: Emergence of CD51-, glycosylphosphatidylinositol-anchor-deficient lymphocytes in rheumatoid arthritis patients following Campath-1H treatment
 AUTHOR(S): Brett, Sara J.; Baxter, Gillian; Cooper, Helen; Rowan, Wendy; Regan, Tessa; Tite, John; Rapson, Nick
 CORPORATE SOURCE: Molecular Immunology Group, Wellcome Research Laboratories, Kent, BR3 3BS, UK
 SOURCE: International Immunology (1996), 8(3), 325-34
 CODEN: INIMEN; ISSN: 0953-8178
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB CD52 is a glycosylinositol-phosphatidyl-inositol (GPI)-linked glycoprotein expressed at high levels on normal T and B lymphocytes and at lower levels on monocytes, while being absent on granulocytes and bone marrow stem cell precursors. The emergence of CD52- lymphocytes of both T and B cell lineages was obsd. in three out of 25 rheumatoid arthritis patients treated with the humanized antibody Campath-1H in phase II clin. trial. Whereas the majority of CD52- B cells had disappeared from the peripheral blood by 3 mo post-treatment, both CD52- CD4+ and CD8+ T cells persisted in the circulation for at least 20 mo. In the two patients that were tested, the GPI-anchored surface mol. CD55 and CD59 were also absent on the CD52- cells, although expression of other cell surface transmembrane proteins (CD3, CD4 and CD2) was unaffected. The CD52- cells maintained a stable phenotype in vitro despite repeated re-stimulation in culture. Both CD52- and CD52+ clones, established from one of the patients, responded to a similar extent to several T cell mitogens, as assessed by proliferation, suggesting that a general defect in expression of GPI-linked mols. does not impair T cell activation. These data show that an immune attack against a GPI-anchored surface mol. can result in the selection of a GPI-anchor-deficient cell population. Despite the persistence of CD52- T cells in the peripheral blood, no adverse reactions assocd. with the presence of these cells were noted in any of the patients; in fact they responded with longer remission times after Campath-1H treatment than the other patients in the trial.

L14 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
 ACCESSION NUMBER: 1996:691799 CAPLUS
 DOCUMENT NUMBER: 126:30101
 TITLE: Monoclonal antibody LR-1 recognizes murine heat-stable antigen, a marker of antigen-presenting cells and developing hematopoietic cells
 AUTHOR(S): Hunt, David W. C.; Jiang, Hui-Jun; Granville, David J.; King, Diane E.; Levy, Julia G.
 CORPORATE SOURCE: Department Microbiology and Immunology, University British Columbia, Vancouver, BC, Can.
 SOURCE: International Archives of Allergy and Immunology (1996), 111(3), 218-228
 CODEN: IAAIEG; ISSN: 1018-2438
 PUBLISHER: Karger
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The rat monoclonal antibody LR-1 was initially described to be reactive with an antigen present on murine splenic B lymphocytes. However, flow-cytometric analyses of cells obtained from thymus, bone marrow, spleen, and lymph nodes showed that LR-1 stained approx. 95, 95, 60-70 and 20%, resp., of cells present within these tissues in normal DBA/2 mice. The marker recognized by LR-1 was present on peripheral erythrocytes and splenic dendritic cells, and activation with lipopolysaccharide A further increased expression of this antigen by splenic B cells. This particular tissue and cellular distribution was similar to that delineated with monoclonal antibodies reactive with heat-stable antigen (HSA). Dual labeling studies were conducted to compare the reactivity patterns of LR-1 and the HSA-reactive monoclonal antibody J11d and indicated that both antibodies recognized splenocytes bearing B cell (IgM) or erythroid (TER-119, CD71) but not T cell (CD4, CD8) markers. Splenocytes exposed to phosphoinositol-specific phospholipase C showed marked redn. in LR-1 binding, indicating that this antibody recognized a glycosylphosphatidylinositol-anchored cell surface protein, consistent with the known structure of HSA. Mixing of LR-1 with the HSA-specific antibodies J11d or M1/69 provided flow-cytometric profiles indistinguishable from those obtained with either antibody alone. However, LR-1 inhibited M1/69 binding to splenocytes by 83%, while J11d reduced M1/69 binding to these cells by only 18%. This finding suggested that LR-1 and M1/69 recognize identical splenic HSA epitopes, while LR-1 and J11d bind distinct antigenic determinants of spleen HSA. Western blot anal. of splenocyte, thymocyte, bone marrow cell and erythrocyte detergent exts. revealed that LR-1 reacted with glycoforms of HSA of known mol. wts. (30-55 kD). Thus, LR-1 recognizes HSA, the murine analog of human CD24, and will be a useful reagent with which to investigate the role of HSA in the immune response and hematopoiesis.

L14 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:486907 CAPLUS
DOCUMENT NUMBER: 125:140041
TITLE: Identification of the sheep homolog of the monocyte cell surface molecule CD14
AUTHOR(S): Gupta, V. K.; McConnell, I.; Dalziel, R. G.; Hopkins, J.
CORPORATE SOURCE: Department of Veterinary Pathology, University of Edinburgh, Summerhall, Edinburgh, EH9 1QH, UK
SOURCE: Veterinary Immunology and Immunopathology (1996), 51(1,2), 89-99
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An ovine monocyte/macrophage cell surface antigen was recognized by 3 mouse monoclonal antibodies (mAbs) VPM65, VPM66, and VPM67. These mAbs also reacted with bovine cells. The antibodies immunopptd. a single, glycosylphosphatidylinositol-linked polypeptide of mol. wt. (Mr) 55,000 which, when deglycosylated, was reduced to Mr 53,000. They reacted strongly with peripheral blood monocytes, alveolar macrophages and peripheral blood granulocytes, and weakly with afferent lymph dendritic cells. They also reacted with macrophages in many different tissues but were non-reactive with lymphocytes. Competitive flow cytometry shows that these 3 mAbs recognize the same or a closely related epitope of a single antigen. An antigen-specific capture ELISA using the anti-human CD14 mAb (TURK4) revealed that all 4 mAbs assoc. with the same antigen. Thus, the mAbs react with the ovine homolog of the lipopolysaccharide (LPS)-LPS binding protein receptor, CD14.

L14 ANSWER 12 OF 42 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5

ACCESSION NUMBER: 95265248 EMBASE
DOCUMENT NUMBER: 1995265248
TITLE: Identification and characterization of a novel protein (p137) which transcytoses bidirectionally in Caco-2 cells.
AUTHOR: Ellis J.A.; Luzio J.P.
CORPORATE SOURCE: Department of Clinical Biochemistry, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QR, United Kingdom
SOURCE: Journal of Biological Chemistry, (1995) 270/35 (20717-20723).
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Antisera raised against detergent-extracted membrane fractions from the human intestinal epithelial cell line Caco-2 were used to screen a human colon cDNA library in a bacteriophage expression vector. This led to the identification, molecular cloning, and sequencing of a novel plasma membrane protein (p137) which was present in approximately equal amounts on the basolateral and apical surfaces of the cell. The pattern of extraction of p137 from membranes by Triton X-114 and its release from membranes after incubation with phosphatidylinositol-specific phospholipase C were consistent with it being a glycosylphosphatidylinositol-anchored membrane protein. Using antibodies raised against bacterial fusion proteins, it was shown that p137 was present on the cell surface as a reducible homodimer of 137 kDa subunits. There was constitutive release of p137 into the culture medium as a non-reducible 280-kDa entity. Pulse-chase experiments showed that newly synthesized p137 appeared at the basolateral side of a Caco-2 cell layer before appearing at the apical domain. Domain-specific surface biotinylation of Caco-2 cells at 4 .degree.C, followed by chasing at 37 .degree.C, demonstrated that p137 is capable of transcytosing in both directions across Caco-2 cells. The unusual plasma membrane domain distribution of this glycosylphosphatidylinositol-linked protein and its transcytosis characteristics demonstrate the existence of a previously uncharacterized apical to basolateral transcytotic pathway in Caco-2 cells.

L14 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6

ACCESSION NUMBER: 1995:805891 CAPLUS
DOCUMENT NUMBER: 123:224310
TITLE: De novo formation of caveolae in lymphocytes by expression of VIP21-caveolin
AUTHOR(S): Fra, Anna M.; Williamson, Edward; Simons, Kai; Parton, Robert G.
CORPORATE SOURCE: European Mol. Biol. Lab., Heidelberg, Germany
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(19), 8655-9
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Caveolae are plasma membrane invaginations, which have been implicated in endothelial transcytosis, endocytosis, potocytosis, and signal transduction. In addn. to their well-defined morphol., caveolae are characterized by the presence of an integral membrane protein termed VIP21-caveolin. The authors have recently obsd. that lymphocytes have no detectable VIP21-caveolin and lack plasma membrane invaginations resembling caveolae. Here the authors transiently express VIP21-caveolin in a lymphocyte cell line using the Semliki Forest virus expression system and show de novo formation of plasma membrane invaginations contg. VIP21-caveolin. These invaginations appear homogeneous in size and morphol. indistinguishable from caveolae of nonlymphoid cells. Moreover, the glycosylphosphatidylinositol-anchored protein Thy1, patched by antibodies, redistributes to the newly formed caveolae. The results show that VIP21-caveolin is a key structural component required for caveolar biogenesis.

L14 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:444475 CAPLUS
DOCUMENT NUMBER: 122:237244

TITLE: Primary structures of CD52
AUTHOR(S): Treumann, Achim; Lifely, M. Robert; Schneider, Pascal;
Ferguson, Michael A. J.
CORPORATE SOURCE: Dep. Biochem., Univ. Dundee, Dundee, DD1 4HN, UK
SOURCE: Journal of Biological Chemistry (1995),
270(11), 6088-99

CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The CD52 antigen was extd. from human spleens with org. solvents and purified by immunoaffinity and reverse-phase chromatog. The latter step resolved two CD52 species, called CD52-I and CD52-II. Both species were found to contain similar N-linked oligosaccharides and glycosylphosphatidylinositol (GPI) anchor glycans. The N-linked oligosaccharides were characterized by methylation linkage anal. and, following exhaustive neuraminidase and endo-.beta.-galactosidase digestion, by the reagent array anal. method. The results showed that the single CD52 N-glycosylation site is occupied by large sialylated, polyacetylosamine-contg., core-fucosylated tetra-antennary oligosaccharides. The locations of the phosphoryl substituents on the GPI anchor glycan were detd. using a new and sensitive method based upon partial acid hydrolysis of the GPI glycan. The difference between CD52-I and CD52-II was in the phosphatidylinositol (PI) moieties of the GPI anchors. The phosphatidylinositol-specific phospholipase C-sensitive CD52-I contained exclusively distearoyl-PI, while the PI-phospholipase C-resistant CD52-II contained predominantly a palmitoylated stearoyl-arachidonoyl-PI, as judged by electrospray ionization mass spectrometry. Tandem mass spectrometric studies indicated that the palmitoyl residue of the CD52-II anchor is attached to the 2-position of the myo-inositol ring. Both the CD52-I and CD52-II PI structures are unusual for GPI anchors and the possible significance of this is discussed. The alkali-lability of the CD52 epitope recognized by the Campath-1H monoclonal antibody was studied. The data suggest that the alkali-labile hydroxyester-linked fatty acids of the GPI anchor are necessary for antibody binding.

L14 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:47622 CAPLUS
DOCUMENT NUMBER: 126:102866

TITLE: Identification of Workshop Endothelial Section mAb that recognize novel glycosyl phosphatidylinositol-anchored antigens

AUTHOR(S): Klickstein, Lloyd B.; York, Michael R.; Luther, Ed;
Springer, Timothy A.

CORPORATE SOURCE: Leucocyte Typing V: White Cell Differentiation
SOURCE: Antigens, Proceedings of the International Workshop and Conference, 5th, Boston, Nov. 3-7, 1993 (1995), Meeting Date 1993, Volume 2, 1850-1852.
Editor(s): Schlossman, Stuart F. Oxford University Press: Oxford, UK.

CODEN: 63WDAC
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The glycosylphosphatidylinositol anchor is a post-translational modification of newly synthesized proteins in which the polypeptide chain is cleaved at a signal sequence near the C-terminal end of the protein and a GPI moiety is transferred to the new C-terminal residue. Here, to identify monoclonal antibodies that recognize novel GPI-anchored antigens, human umbilical cord vein endothelial cells (HUVEC), with and without phosphatidylinositol-specific phospholipase C treatment, were analyzed by indirect immunofluorescence and flow cytometry.

L14 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:47453 CAPLUS
DOCUMENT NUMBER: 126:116717

TITLE: Identification of novel GPI-anchored antigens by analysis of GPI-anchor-deficient cells with mAb in the Blind Panel

AUTHOR(S): Klickstein, Lloyd B.; York, Michael R.; Luther, Ed;
Springer, Timothy A.

CORPORATE SOURCE: Leucocyte Typing V: White Cell Differentiation
SOURCE: Antigens, Proceedings of the International Workshop and Conference, 5th, Boston, Nov. 3-7, 1993 (1995), Meeting Date 1993, Volume 2, 1478-1481.
Editor(s): Schlossman, Stuart F. Oxford University Press: Oxford, UK.

CODEN: 63WDAC
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Studies with various cell lines, GPI-anchor-deficient cell lines, phospholipase C-treated cells, and monoclonal antibodies from the Fifth International Workshop on Human Leukocyte Antigens indicated that CD93, CD58, CDw108, CDw109, CDw75, and CDw76 are GPI anchored antigens. Antigens A049 (3F4), T010 (4dD8), and E057 (C4A9.2.3) also appear to be GPI anchored.

L14 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:47453 CAPLUS

DOCUMENT NUMBER: 126:102832
TITLE: Adhesion structure subpanel 1, E rosetting/GPI anchor:
CD2, CD48, CD55, CD58, CDS9, CD99, and CDw108
AUTHOR(S): Klickstein, Lloyd B.; Springer, Timothy A.
CORPORATE SOURCE: UK
SOURCE: Leucocyte Typing V: White Cell Differentiation
Antigens, Proceedings of the International Workshop
and Conference, 5th, Boston, Nov. 3-7, 1993 (1995),
Meeting Date 1993, Volume 2, 1468-1471.
Editor(s): Schlossman, Stuart F. Oxford University
Press: Oxford, UK.
CODEN: 63WDAC

DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors report cluster anal. and isotype for mouse and rat monoclonal antibodies to GPI-anchored surface antigens mediating adhesion. In addn., the authors exmd. the effect of these antibodies on PBMC proliferation.

L14 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 1995:684499 CAPLUS
DOCUMENT NUMBER: 123:225436
TITLE: Investigations using a novel monoclonal antibody to the glycosylphosphatidylinositol-anchored protein that carries Gregory, Holley, and Dombrock blood group antigens
AUTHOR(S): Rao, N.; Udani, M.; Nelson, J.; Reid, M. E.; Telen, M. J.
CORPORATE SOURCE: Medical Center, Duke University, Durham, NC, USA
SOURCE: Transfusion (Bethesda, Maryland) (1995), 35(6), 459-64
PUBLISHER: American Association of Blood Banks
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The high-frequency Hy and Gya antigens have been shown to reside on the same protein. Gy(a-) Hy-neg. red cells are also Do(a-b'). A mouse monoclonal antibody, 5B10, was produced with specificity related to the human Gregory, Holley, and Dombrock blood group antigens. The antibody reacted in direct hemagglutination assays, and its specificity was investigated by RIA, inhibition assay, and Western blotting. The 5B10 antibody failed to bind to abnormal paroxysmal nocturnal hemoglobinuria red cells and human erythroleukemia cell line K562, but it was weakly reactive with HEL cells. Red cells, but not other circulating hematopoietic cells, express the 5B10 antigen. The 5B10 antibody had a specificity similar but not identical to that of Gya. Gy(a-) Hy-neg. red cells reacted extremely weakly with 5B10 antibody, but Gy(a-) Hy-neg. red cells treated with a variety of proteases bound 5B10 antibody strongly. This suggests that these cells express a variant form of the protein recognized by 5B10. Identification of a monoclonal antibody to this glycosylphosphatidylinositol-linked protein opens a new avenue for investigation of the biochem., genetics, and function of the glycosylphosphatidylinositol-linked protein that bears the Gya, Hy, and Do antigens.

L14 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:523941 CAPLUS
DOCUMENT NUMBER: 123:77430
TITLE: Schistosoma mansoni: molecular cloning and sequencing of the 200-kDa chemotherapeutic target antigen
AUTHOR(S): Hall, Traci M.; Tanaka, Joseph; Gerald T.; Strand, Mette
CORPORATE SOURCE: School of Medicine, Johns Hopkins University, Baltimore, MD, 21205, USA
SOURCE: Experimental Parasitology (1995), 80(2), 242-9
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Praziquantel is the drug of choice for human schistosomiasis. The efficacy of this drug is impaired in immune-deficient mice. However, transfer to B cell-depleted mice of a monoclonal antibody that recognizes a 200-kDa GPI-anchored glycoprotein of S. mansoni restores the effectiveness of praziquantel. In order to characterize this target antigen, we have isolated and sequenced cDNA clones encoding the 200-kDa protein. Three overlapping cDNA clones contained the complete nucleotide sequence. The sequences of five tryptic peptides from the native 200-kDa protein could be matched with regions in the amino acid sequence deduced from the nucleotide sequence of the isolated clones. This deduced amino acid sequence differed from sequences available in six databases. Praziquantel exposes epitopes on the worm surface that are normally not exposed, and we have shown by immunofluorescent staining that the fusion protein encoded by one of our cDNA clones expresses epitopes that are exposed on the surface of praziquantel-treated worms.

L14 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:406856 CAPLUS
DOCUMENT NUMBER: 121:6856
TITLE: An epitope on carcinoembryonic antigen defined by the clinically relevant antibody PR1A3
AUTHOR(S): Durbin, Helga; Young, Susan; Stewart, Lorna M.; Wrba, Fritz; Rowan, Andrew J.; Snary, David; Bodmer, Walter E.
CORPORATE SOURCE: Cancer Genet. Lab., Imp. Cancer Res. Fund, London, WC2A 3PX, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(10), 4313-17
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The monoclonal antibody PR1A3 has been used successfully for in vivo imaging of colorectal cancers, and several properties assocd. with this antibody, including minimal reactions of the antibody with circulating antigen in patients' sera, differentiate it from anti-carcinoembryonic antigen (CEA) antibodies used in similar studies. However, the antigen bound by PR1A3 was identified as CEA by anal. of somatic cell hybrids and by antigen expression from yeast artificial chromosomes, cosmids, and cDNA clones. The mol. wt., presence of a glycosylphosphatidylinositol anchor, elevation of surface expression of γ -interferon, and N-terminal amino acid sequence all confirmed the antigen identification as CEA. A series of biliary glycoprotein-CEA hybrid proteins was produced which demonstrated that the epitope bound by the antibody was at the site of

membrane attachment and involved parts of the glycosylphosphatidylinositol anchor and the B3 domain of CEA to form a conformational epitope. Access to this epitope, although possible when the antigen was on the cell surface, appeared to be blocked when CEA was released from the cell. The nature and location of the epitope on CEA are proposed to be responsible for the unique properties of the antibody.

L14 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:242358 CAPLUS
DOCUMENT NUMBER: 122:7931
TITLE: Recombinant glycosylphosphatidylinositol-anchored proteins are not associated with protein kinases in transfected thymoma cells
AUTHOR(S): Clissold, Patricia M.
CORPORATE SOURCE: Molecular Immunopathology Unit, MRC Centre, Cambridge, CB2, 2QH, UK
SOURCE: Biochemical Journal (1994), 304(3), 853-9
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crosslinking by antibody of some glycosylphosphatidylinositol (GPI)-anchored proteins on the plasma membrane of T cells leads to cell activation. Phosphorylation of proteins on tyrosine residues has a central role in the control of T cell activation, and non-receptor protein tyrosine kinases can be copptd. with immune complexes of GPI-anchored proteins in T cell lysates. To investigate the nature of this interaction, two recombinant GPI-anchored proteins were constructed (using the GPI signal sequence from Thy-1), and their assocns. with protein tyrosine kinases in stable transfectants of a mouse thymoma have been investigated. One recombinant GPI protein is the extracellular domain of the human complement receptor-1, normally an integral membrane protein, and the other is the secreted protein, human tissue inhibitor of human metalloproteinases. The latter protein should be foreign to the cell surface and yet has been expressed as a GPI-anchored protein at levels equiv. to the highly expressed antigens Thy-1 and Ly6 A2 on mouse thymoma cells. Neither of the two recombinant proteins, when immunopptd. from NP-40 lysates of transfected cells, were assocd. with protein tyrosine kinases in contrast with the natural endogenous GPI-anchored proteins Thy-1 and Ly6.A2 in non-transfected parental cells. Moreover, high expression of foreign recombinant GPI protein appears to interfere with the assocn. of the natural GPI proteins with protein tyrosine kinases.

L14 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:242361 CAPLUS
DOCUMENT NUMBER: 122:7553
TITLE: Lytic anti-.alpha.-galactosyl antibodies from patients with chronic Chagas' disease, recognize novel O-linked oligosaccharides on mucin-like glycosyl-phosphatidylinositol-anchored glycoproteins of Trypanosoma cruzi
AUTHOR(S): Almeida, Igor C.; Ferguson, Michael A.; Schenkman, Sergio; Travassos, Luiz R.
CORPORATE SOURCE: Disciplina de Biol. Celular, Esc. Paulista de Medicina, Sao Paulo, SP 04023-062, Brazil
SOURCE: Biochemical Journal (1994), 304(3), 793-802
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sera of patients with chronic Chagas' disease (American trypanosomiasis) contain elevated levels of anti-.alpha.-galactosyl antibodies that are lytic to *Trypanosoma cruzi*. The *T. cruzi* trypomastigote F2/3 antigen complex recognized by these antibodies runs as a broad smear on SDS-PAGE. Treatment of *T. cruzi* trypomastigote cells with bacterial phosphatidylinositol-specific phospholipase C (PI-PLC) abolished most of their reactivity to chagasic anti-.alpha.-galactosyl antibodies (anti-Gal). The F2/3 antigen complex, purified by solvent extn. and hydrophobic-interaction chromatog., contained 60% carbohydrate by wt. and substantial amts. of Thr, Ser, Glx, Asx, Gly, Ala and Pro, but relatively few hydrophobic amino acids. The presence of myo-inositol, ethanolamine and 1-O-hexadecylglycerol suggested the presence of glycosyl-phosphatidylinositol membrane anchors. This was confirmed by PI-PLC treatment, which rendered the F2/3 mols. hydrophilic and reactive to anti-(cross-reaching determinant) antibodies. The majority of the GlcNAc content of the F2/3 antigens was found at the reducing termini of oligosaccharides in O-glycosidic linkage to Thr residues. These O-linked oligosaccharides could be released by .beta.-elimination and by mild hydrazinolysis. The smallest released oligosaccharitol that was reactive with the chagasic anti-Gal was Gal.alpha.1-3Gal.beta.1-4GlcNAcol (where GlcNAcol is N-acetylglucosaminitol). Several other Gal-contg. oligosaccharitols were obsd., most of which were branched and contained 4,6-di-O-substituted GlcNAcol at their reducing termini. About half of the total released oligosaccharitols could bind to immobilized chagasic anti-Gal, but none of the bound to the anti-Gal isolated from normal human sera. These data suggest that the specificities of the chagasic anti-Gal are quite different from the natural anti-Gal isolated from normal human sera. Therefore, these novel *T. cruzi* O-linked oligosaccharides are highly immunogenic under the conditions of natural infection and are the targets for lytic chagasic anti-Gal.

L14 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1994:103099 CAPLUS
DOCUMENT NUMBER: 120:103099
TITLE: Expression and secretion of glycosylphosphatidylinositol-specific phospholipase D by myeloid cell lines
AUTHOR(S): Xie, Mingsheng; Low, Martin G.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Biochemical Journal (1994), 297(3), 547-54
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB All the myeloid cell lines tested, including K562 (multipotential blast), KG-1 (human myeloblast), HL-60, NB4, PLB-985 (human promyelocyte), U937 (human promonocyte), THP-1 (human monocyte) and J774, RAW264.7 (mouse monocyte/macrophage), contained glycosylphosphatidylinositol (GPI)-degrading activity. TLC anal. of reaction products confirmed the activity as a phospholipase D (PLD). These cells also exhibited pos. immunofluorescent staining with an anti-GPI-PLD monoclonal antibody. The expression of GPI-PLD activity was not

substantially reduced when the cells were cultured in either serum-free medium or GPI-PLD-depleted regular medium. Both granulocytic and monocytic differentiation of myelomonoblastic lines (e.g. HL-60) induced by DMSO or phorbol ester, resp., was accompanied by a 2-3-fold increase in GPI-PLD activity. J774 and HL-60 cells secreted GPI-PLD into the medium constitutively. Taken together, these data suggest that myeloid cells are a potential contributor to the circulating GPI-PLD pool. As leukocytes express many important GPI-anchored surface antigens, these cells may prove to be valuable model system for studying the physiol. functions of GPI-PLD.

L14 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:320921 CAPLUS
DOCUMENT NUMBER: 120:320921
TITLE: GPI-anchored glycoconjugates from *Trypanosoma cruzi* trypomastigotes are recognized by lytic anti-.alpha.-galactosyl antibodies isolated from patients with chronic Chagas' disease
AUTHOR(S): Almeida, I.C.; Ferguson, M.A.J.; Schenkman, S.; Travassos, L.R.
CORPORATE SOURCE: Discip. de Biol. Cel., Esc. Paul. de Med., Sao Paulo, 04023-062, Brazil
SOURCE: Brazilian Journal of Medical and Biological Research (1994), 27(2), 443-7
CODEN: BJMRDK; ISSN: 0100-879X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The target mols. on the cell surface of *Trypanosoma cruzi* trypomastigotes reacting with lytic anti-.alpha.-galactosyl antibodies from chronic patients with Chagas' disease (Ch anti-Gal) have been purified by solvent extrn. and identified as glycoconjugates migrating in the 74-96-kDa range (F2 antigen) and in the 120-200-kDa range (F3 antigen) on SDS-PAGE. The F3 antigen was tested for binding to Ch and normal human serum (NHS) anti-Gal and to MoAb 3C9. The authors obstd. that Ch anti-Gal and MoAb 3C9, but not NHS anti-Gal, bind strongly to the trypomastigote glycoconjugates. These antibodies, however, did not compete with each other for binding to F3 mols., indicating that they are recognizing different epitopes. Binding of Ch anti-Gal to F3 antigen is abolished by treatment of these mols. with .alpha.- but not .beta.-galactosidase. Binding of 3C9 MoAb is abolished by treatment of F3 with sialidase. F2/F3 antigens absorbed Ch anti-Gal as well as lytic antibodies from total chagasic sera. These antigens also specifically discriminate between the serum reactivity of patients with active Chagas' disease and those of sera from cured patients, drug-treated patients with dissoccd. serol. (pos. conventional serol., neg. trypanolytic activity), healthy individuals, and patients with several other infectious diseases. The authors also obstd. that F2/F3 antigens are anchored to the parasite membrane via glycosylinositolphosphatidylinositol (GPI). The .alpha.-galactosyl epitopes recognized by Ch anti-Gal are present in a series of O-linked oligosaccharide chains in the mucin-like glycoprotein component of the complex.

L14 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1994:320799 CAPLUS
DOCUMENT NUMBER: 120:320799
TITLE: Early molecular signals induced by antibodies to GPI-anchored proteins
AUTHOR(S): Robinson, P.; Hederer, R.
CORPORATE SOURCE: Transplant. Biol. Sect., Clin. Res. Cent., Harrow/Middlesex, HA1 3UJ, UK
SOURCE: Brazilian Journal of Medical and Biological Research (1994), 27(2), 263-7
CODEN: BJMRDK; ISSN: 0100-879X
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 10 refs. The authors have examd. intracellular biochem. and metabolic changes induced by antibodies specific for glycosylinositolphosphatidylinositol (GPI)-anchored cell surface mols. In lymphoid cells the earliest detectable responses are phosphorylation of intracellular substrates. The GPI-linked target antigens are also rapidly redistributed into patches and caps on the cell surface and then internalized. Between two and five hours later, cytokine receptors are expressed. Later, cells become metabolically active and begin to proliferate and express endogenous cytokines, thus promoting autocrine growth. Very early events, such as kinase activity, are induced by antibody binding alone and are characteristic of the cell surface mol. recognized by antibodies. Thus, the initial events in the activation cascade are crit. in selecting the metabolic route. Progression down the activation cascade requires further signals such as crosslinking antibodies, exogenous cytokines, phorbol esters, or accessory cells. Once in cycle, cells no longer display evidence of their original route of activation. Activated T lymphocytes acquire resistance to cleavage by GPI-specific phospholipase C, suggesting a possible feedback mechanism to limit cell proliferation.

L14 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1994:6423 CAPLUS
DOCUMENT NUMBER: 120:6423
TITLE: Activation of human monocytes and granulocytes by monoclonal antibodies to glycosylinositolphosphatidylinositol-anchored antigens
AUTHOR(S): Lund-Johansen, Fridtjof; Olweus, Johanna; Symington, Frank W.; Aarli, Aanen; Thompson, John S.; Vilella, Ramon; Skubitz, Keith; Horejsi, Vaclav
CORPORATE SOURCE: Univ. Bergen, Gade Inst., Bergen, Norway
SOURCE: European Journal of Immunology (1993), 23(11), 2782-91
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigated possible receptor-like characteristics of glycosylinositolphosphatidylinositol (GPI)-linked antigens on human monocytes and granulocytes by measuring cytoplasmic calcium fluxes and the oxidative burst in cells following crosslinking of GPI-linked antigens. Crosslinking of cell-bound anti-CD14, -CDw52 and -CD55 induced cytoplasmic calcium fluxes and oxidative bursts in unprimed human monocytes similar to those obstd. following Fc-gamma.R crosslinking. In granulocytes primed with 200 nM N-formyl-Met-Leu-Phe (FMLP), crosslinking of cell-bound anti-CD16, -CD24, -CD59 and -CD67 led to calcium fluxes and activation of the oxidative burst. The oxidative bursts mediated by GPI-linked antigens were stronger than those induced by 200 nM FMLP, even though FMLP induced a larger increase in cytoplasmic calcium concn. The responses were likely to be independent of Fc-gamma.R interactions as F(ab')2 fragments of IgG

or IgM antibodies were used in the expts. Activating effects of monoclonal antibody to GPI-linked antigens were not obstd. in cells from patients with paroxysmal nocturnal hemoglobinuria, which are deficient in GPI-linked antigens. In addn., treatment with GPI-specific phospholipase C led to inhibition of cell activation through GPI-linked antigens but not through transmembrane receptors. Crosslinking of a no. of non-GPI-linked antigens (CD11a, CD18, CD31, CD35, CD43, and CD45) neither induced calcium fluxes, nor activated the oxidative burst. The results indicate that most, if not all, GPI-linked surface glycoproteins on myeloid cells are capable of mediating cell activation and suggest that the GPI anchor is a structure facilitating signal transduction.

L14 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:620203 CAPLUS
 DOCUMENT NUMBER: 119:220203
 TITLE: Rapid purification of glycosyl-phosphatidylinositol-anchored alkaline phosphatase from human neutrophils after up-regulation to the cell surface
 AUTHOR(S): Cain, Timothy J.; Liu, Youjiang; Kobayashi, Toshihiro; Robinson, John M.
 CORPORATE SOURCE: Dep. Cell Biol. Neurobiol. Anat., Ohio State Univ., Columbus, OH, 43210, USA
 SOURCE: Journal of Histochemistry and Cytochemistry (1993), 41(9), 1367-72
 CODEN: JHCVAS; ISSN: 0022-1554
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Alk. phosphatase (APase) belongs to a growing family of membrane-assocd. proteins tethered to the lipid bilayer via a glycosyl-phosphatidylinositol (GPI) anchor. Human neutrophils contain an intracellular pool of APase assocd. with a novel membrane-bound compartment. Stimulation of neutrophils with the chemotactic peptide formyl-Met-Leu-Phe (fMLP) leads to rapid up-regulation of essentially all of the APase to sites in continuity with the extracellular medium. Pre-treatment of neutrophils with cytochalasin B (cyto B) followed by fMLP likewise leads to expression of the enzyme on the cell surface and a dramatic alteration in cell morphol., but subsequent internalization of the plasmalemma is minimized. Pre-treatment with cyto B and fMLP has been used for isolation and purifn. of neutrophil APase. Specifically, neutrophils were treated with phosphatidylinositol-specific phospholipase C to release GPI-anchored proteins from the cell surface. APase was purified from supernatants of these preps. by electrophoresis in a non-denaturing gel system and subsequent electroelution. With this approach the authors rapidly purified neutrophil APase to homogeneity; this protein was then used for immunization. Immunoblotting, ELISA, and immunocytochem. localization were used to characterize the resulting antibodies.

L14 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:406801 CAPLUS
 DOCUMENT NUMBER: 119:6801
 TITLE: A monoclonal antibody reactive with a glycosophatidylinositol-anchored molecule on T cells defines CD4+ T cell subsets
 AUTHOR(S): Nagata, Norikazu; Taketani, Shigeru; Adachi, Yasushi; Hosaka, Naoki; Miyashima, Shigeo; Tokunaga, Rikio; Ikebara, Susumu
 CORPORATE SOURCE: 1st Dep. Pathol., Kansai Med. Univ., Moriguchi, Japan
 SOURCE: European Journal of Immunology (1993), 23(5), 1193-6
 CODEN: EJIMAF; ISSN: 0014-2980
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A hybridoma, 25T3 (IgM, .kappa.), was established from MRL/+ mice immunized with an autoreactive T cell line (1+/+ T1). The reactivity of the antigen (Ag) recognized by hybridoma 25T3 (25T3-Ag) expressed on thymic and splenic cells was abolished by treatment with phosphatidylinositol-specific phospholipase C, showing that 25T3-Ag is a glycosophatidylinositol-anchored Ag. The 25T3-Ag was expressed on approx. 90% of thymocytes. Double-neg., double-pos. and CD8 single-pos. cells were highly pos. for the expression of 25T3-Ag, whereas CD4 single-pos. cells were weakly pos. (approx. 40%) or neg. (approx. 60%). In the spleen, only CD3+ cells (and not B220+ nor Mac-1+ cells) reacted with 25T3 monoclonal antibody (mab), indicating that 25T3 mAb is specific for T cells. The majority of splenic CD8+ T cells were pos. for the expression of 25T3-Ag, although the intensity was weaker than that of thymocytes. In contrast, splenic CD4+ T cells were divided into neg. (60-70%) and pos. (30-40%) populations. Similar staining profiles were obstd. in BALB/c, C57BL/6, C3H/HeN and AKR/J mice. When BALB/c CD4+ T cell subsets were sorted and cultured with irradiated (25 Gy) antigen-presenting cells, stimulation with immobilized anti-CD3 mAb for 2 days resulted in CD4+25T3+ cells secreting more interleukin-2 and less interleukin-4 than did CD4+25T3- subsets, although the proliferative responses of the cells on day 2 of culture were similar. This suggests that CD4+ T cells can be divided into two populations and relatively defined as T helper 1 and T helper 2 cells using this 25T3 mab. Immunoppt. and SDS-PAGE revealed that 25T3-Ag was approx. 70 kD. These findings are discussed in relation to CD4+ T cell subsets.

L14 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
 ACCESSION NUMBER: 1994:5419 CAPLUS
 DOCUMENT NUMBER: 120:5419
 TITLE: Glycosylphosphatidylinositol-specific phospholipase D is localized in keratinocytes
 AUTHOR(S): Xie, Mingsheng; Seiko, Ann M.; Low, Martin G.
 CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
 SOURCE: American Journal of Physiology (1993), 265(4, Pt. 2), C1156-C1168
 CODEN: AJPHAP; ISSN: 0002-9513
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Glycosylphosphatidylinositol-specific phospholipase D (GPI-PLD) is abundant in mammalian plasma, but little is known of its cellular and tissue distribution. In this study frozen sections of perfused tissues from adult rats were stained with monoclonal antibodies against GPI-PLD. The most intense staining was obstd. in the stratified squamous epithelium of the forestomach. Staining was also obstd. in the esophagus, the tongue, the hard palate, and the skin but not in most other tissues including the columnar epithelium of the stomach or the lower gastrointestinal tract. GPI-PLD expression was also detected in several keratinocyte cell lines. Biochem. assays of glycosylphosphatidylinositol-degrading activity using [³H]myristate-labeled variant surface glycoprotein as substrate provided independent

evidence for the presence of GPI-PLD. Expression of GPI-PLD by keratinocytes was not affected by culture in serum-free media, indicating that it does not originate by uptake of serum GPI-PLD in the media. These data suggest that keratinocytes are an important site of action of GPI-PLD and possibly a contributor to the plasma GPI-PLD pool.

L14 ANSWER 30 OF 42 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 12
ACCESSION NUMBER: 94038320 EMBASE
DOCUMENT NUMBER: 1994038320
TITLE: Neutralizing monoclonal antibodies to glycosylphosphatidylinositol, the dominant TNF-.alpha.-inducing toxin of Plasmodium falciparum: Prospects for the immunotherapy of severe malaria.
AUTHOR: Schofield L.; Vivas L.; Hackett F.; Gerold P.; Schwartz R.T.; Tachado S.
CORPORATE SOURCE: National Inst for Medical Research, Mill Hill, London NW7 1AA, United Kingdom
SOURCE: Annals of Tropical Medicine and Parasitology, (1993) 87/6 (617-626).
ISSN: 0003-4983 CODEN: ATMPA2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tumour necrosis factor-.alpha. (TNF-.alpha.) is an endogenous mediator of shock and inflammation. Many of the life-threatening and severe pathologies associated with complicated and cerebral malaria are thought to result from the overproduction of this cytokine in response to agents of parasite origin. The identification and characterization of these agents may therefore provide the molecular basis for a detailed understanding of the disease process. Recently it has been shown that glycosylphosphatidylinositols are a novel class of glycolipid toxin produced by the parasite, which substitute for the endogenous inositolglycan-based signal transduction pathways of the host. Glycosylphosphatidylinositol stimulates high levels of TNF-.alpha. and interleukin-1 production by macrophages and induces hypoglycaemia through an insulin-mimetic activity, and may therefore contribute to the cerebral syndrome and other malarial pathophysiology. That monoclonal antibodies to parasite-derived glycosylphosphatidylinositol** can neutralize the toxic activities of whole parasite extracts is also demonstrated here. These findings suggest a central role for glycosylphosphatidylinositol of parasite origin in the aetiology of severe malaria and suggest novel approaches for the immunotherapy or immunoprophylaxis of disease.

L14 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1993:75619 CAPLUS
DOCUMENT NUMBER: 118:75619
TITLE: Membrane insertion and ***antibody recognition of a glycosylphosphatidylinositol-anchored protein: an optical study
AUTHOR(S): Ramsden, J. J.; Schneider, P.
CORPORATE SOURCE: Dep. Biophys. Chem., Biozentrum, Basel, 4056, Switz.
SOURCE: Biochemistry (1993), 32(2), 523-9
CODEN: BICBWA; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kinetics of binding of a glycolipid-anchored protein (the promastigote surface protease, PSP) to planar lecithin bilayers is studied by an integrated optics technique, in which the bilayer membrane is supported on an optical wave guide and the phase velocities of guided light modes in the wave guide are measured. From these velocities, the optical parameters of the membrane and PSP layers deposited on the wave guide are detd., yielding in particular the mass of PSP bound to the membrane, which is followed in real time. From a comparison of the binding rates of PSP and PSP from which the lipid moiety has been removed, it is shown that the lipid moiety plays a key role in anchoring the protein to the membrane. Specific and nonspecific binding of antibodies to membrane-anchored PSP is also investigated. As little as a fifth of a monolayer of PSP is sufficient to suppress the appreciable nonspecific binding of antibodies to the membrane.

L14 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:629485 CAPLUS
DOCUMENT NUMBER: 117:229485
TITLE: Immunolocalization of a glycosylphosphatidylinositol-specific phospholipase D in mast cells found in normal tissue and neurofibromatosis lesions
AUTHOR(S): Metz, Christine N.; Thomas, Patricia; Davitz, Michael A.
CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, USA
SOURCE: American Journal of Pathology (1992), 140(6), 1275-81
CODEN: AJPA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A large no. of eukaryotic proteins have been shown to be anchored to the cell membrane by glycosylphosphatidylinositol (GPI). This glycolipid anchor can serve as a substrate for anchor-specific phospholipases that convert the GPI-anchored membrane proteins into sol. forms. Sol. forms of many GPI anchored proteins have been identified in vivo in connective tissue, plasma, and urine. The authors have discovered that mammalian plasma contains a GPI-specific phospholipase D (GPI-PLD). Because it recognizes a portion of the conserved glycan core structure, all GPI-anchored proteins are potential substrates. The authors report the development of a murine monoclonal antibody specific for one form of the human GPI-PLD and the immunohistochem. localization of this enzyme to mast cells.

L14 ANSWER 33 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:462022 BIOSIS
DOCUMENT NUMBER: BR43:83372
TITLE: PAROXYSMAL NOCTURNAL HEMOGLOBINURIA DIAGNOSIS WITH THE FLUORESCENCE-ACTIVATED CELL SORTER.
AUTHOR(S): SCHUBERT J; SCHMIDT R E
CORPORATE SOURCE: ABT. KLINISCHE IMMUNOL., ZENTRUM INNERE MED. DERMATOL., MEDIZINISCHE HOCHSCHULE, KONSTANTY-GUTSCHOW-STR. 8, W-3000 HANNOVER 61.
SOURCE: DMW, Dtsch. Med. Wochenschr., (1992) 117 (25), 985-989.
CODEN: DDMWDP. ISSN: 0012-0472.

FILE SEGMENT: BR; OLD
LANGUAGE: German

L14 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:468166 CAPLUS
DOCUMENT NUMBER: 117:68166
TITLE: Purification and characterization of antibodies to the glycosylphosphatidylinositol anchor of human membrane dipeptidase
AUTHOR(S): Broomfield, Samantha J.; Hooper, Nigel M.
CORPORATE SOURCE: Dep. Biochem. Mol. Biol., Univ. Leeds, Leeds, LS2 9JT, UK
SOURCE: Biochemical Society Transactions (1992), 20(2), 118S
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By affinity chromatog. on immobilized phosphatidylinositol-specific phospholipase C solubilized aminopeptidase P, a cross-reacting determinant (CRD)-specific antiserum, RH177/S, was purified from a crude antiserum raised to the phosphatidylinositol-specific phospholipase C solubilized form of human kidney dipeptidase. This antiserum was shown, by Western blotting and an ELISA, to recognize other G-PI anchored proteins, the major epitope being the inositol 1,2-monophosphate formed on phospholipase C cleavage of the anchor. Recognition by RH177/S may also involve a minor epitope, possibly a substituent on the inositol ring or the glucosamine residue which is resistant to mild acid treatment. Purifn. of CRD-specific antibodies by a second method with membrane-form dipeptidase immobilized on nitrocellulose was unsuccessful.

L14 ANSWER 35 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:468061 BIOSIS
DOCUMENT NUMBER: BR43:89411
TITLE: MONOClonAL ANTIBODIES AGAINST GLYCOSYLPHOSPHATIDYLINOSITOL-SPECIFIC PHOSPHOLIPASE D.
AUTHOR(S): LIAO J; HONER M; MORTENSEN V; KOCH C; NORGAARD-PEDERSEN B; BRODEBECK U
CORPORATE SOURCE: INSTITUTE BIOCHEMISTRY MOLECULAR BIOLOGY, UNIVERSITY BERN, SWITZ.
SOURCE: 24TH ANNUAL MEETING OF THE SWISS SOCIETIES FOR EXPERIMENTAL BIOLOGY (USGB/USSBE), BASEL, SWITZERLAND, MARCH 19-20, 1992. EXPERIENTIA (BASEL), (1992) 48 (ABSTR), A19.
CODEN: EXPEAM. ISSN: 0014-4754.

DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
L14 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:629904 CAPLUS
DOCUMENT NUMBER: 115:229904
TITLE: Evidence of synergy between Thy-1 and CD3/TCR complex in signal delivery to murine thymocytes for cell death
AUTHOR(S): Nakashima, Izumi; Zhang, Yue Hua; Rahman, S. M. Jamshedur, Yoshida, Tomoaki; Isobe, Kenichi; Ding, Linna; Iwamoto, Takashi; Hamaguchi, Michinari; Ikezawa, Hiroh; Taguchi, Ryo
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Journal of Immunology (1991), 147(4), 1153-62
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential role of Thy-1 in CD3/TCR complex-mediated signal delivery to murine thymocytes was studied. Antigen (Ag)-mimicking cross-linked anti-CD3 mab stimulated suspension of thymocytes from adult (6-8 wk old) mice for a brisk free cytoplasmic calcium ion ($[Ca^{2+}]_i$) rise, low level of inositol phosphate prodn., and marginal increase in tyrosine-specific phosphorylation of 110/120-kDa and 40-kDa cellular proteins. Weak but sustained $[Ca^{2+}]_i$ rise, low inositol phosphate prodn., and weak protein tyrosine phosphorylation were also induced by the cross-linked anti-Thy-1 mab that mimicked the putative natural ligand. The signal delivered via either of these two pathways was however insufficient for definitively promoting cell death and DNA fragmentation in the adult thymocytes. Here it is demonstrated that anti-Thy-1 mAb synergized with anti-CD3 mAb for inducing a long-lasting prominent $[Ca^{2+}]_i$ rise, definite inositol 1,4,5-triphosphate and inositol 1,3,4,5-tetrakiphosphate prodn., and extensive tyrosine-specific phosphorylation of 110/120-, 92-, 75-, and 40-kDa proteins, which resulted in marked promotion of cell death and DNA fragmentation in the adult thymocytes. This unique anti-Thy-1 antibody activity was directed to glycosylphosphatidylinosito 1-anchored Thy-1, and was distinguished from the known anti-LST4 activity that augmented the CD3-mediated signal transduction in a different manner. The synergistic actions of anti-CD3 and anti-Thy-1 mAb obligatorily required the crosslinking of the two mAb together. The anti-CD3 and anti-Thy-1 mAb cross-linked together acted on immature thymocytes from newborn (<24 h after birth) mice for more extensive promotion of protein tyrosine phosphorylation and cell death. In addn., they affected peripheral T lymphocytes for accelerating protein tyrosine phosphorylation but not cell death. These results suggest a novel function of glycosylphosphatidylinositol-anchored Thy-1 as a possible unique intrathymic intensifier of the CD3/TCR complex-delivered signal for neg. thymocyte selection.

L14 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:18698 CAPLUS
DOCUMENT NUMBER: 116:18698
TITLE: Signal transduction by GPI-anchored membrane proteins
AUTHOR(S): Robinson, Peter J.
CORPORATE SOURCE: Transplant. Biol. Sect., Clin. Res. Cent., Harrow, UK
SOURCE: Cell Biology International Reports (1991), 15(9), 761-7
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 16 refs., of the role of glycosyl-phosphatidylinositol (GPI) -anchored membrane proteins and antibodies to them in signal transduction. Functions of GPI anchors, their role in activation of lymphocytes, mol. assocns. on the cell surface involving these anchors, and cell surface mobility and signaling are topics included.

L14 ANSWER 38 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1991:136813 BIOSIS
DOCUMENT NUMBER: BA91:73353
TITLE: CHARACTERIZATION OF ANTIBODIES TO THE GLYCOSYLPHOSPHATIDYLINOSITOL MEMBRANE ANCHORS OF MAMMALIAN PROTEINS.
AUTHOR(S): HOOPER N M; BROOMFIELD S J; TURNER A J
CORPORATE SOURCE: MEMBRANE PEPTIDASE RES. GROUP, DEP. BIOCHEM. AND MOLECULAR BIOL., UNIV. LEEDS, LEEDS LS2 9JT, UK.
SOURCE: BIOCHEM J, (1991) 273 (2), 301-306.
CODEN: BIJOAK. ISSN: 0306-3275.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Two polyclonal antisera were raised in rabbits to the phospholipase C-solubilized forms of pig renal dipeptidase (EC 3.4.13.11) and pig aminopeptidase P (EC 3.4.11.9). These antisera were purified and shown to cross-react with other glycosyl-phosphatidylinositol (G-PI)-anchored proteins isolated from pig, human and trypanosomes. The epitopes involved in this cross-reactivity were characterized by Western-blot analysis after mild acid or nitrous acid treatment of the G-PI-anchored proteins and by a competitive (ELISA) with other G-PI-anchored proteins and individual components of the anchor structure. These studies revealed that the primary epitope for both antisera is the inositol 1,2-(cyclic)monophosphate that is formed on phospholipase C cleavage of the intact G-PI anchor. Other minor epitopes, such as phosphoethanolamine, probably involve side-chain modifications to the core anchor structure that may be species-specific.

L14 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14
ACCESSION NUMBER: 1991:605569 CAPLUS
DOCUMENT NUMBER: 115:205559
TITLE: Production of monoclonal antibodies against the purified glycosylphosphatidylinositol anchor of the variant surface glycoprotein from Trypanosoma brucei brucei.
AUTHOR(S): Preuss, Ute; Schuler, Frank; Peter-Katalinic, Jasna; Gunawan, Johannes; Egge, Heinz
CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Bonn, Bonn, W-5300/1, Germany
SOURCE: Archives of Biochemistry and Biophysics (1991), 291(1), 139-46
CODEN: ABBI4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The glycosylphosphatidylinositol anchor (GPI) from the membrane form variant surface glycoprotein (mfVSG) of T. brucei brucei was isolated and identified after radioactive labeling with [³H]myristic acid, by immunostaining on HPLC with a polyclonal antibody directed against mfVSG, and by neg. ion laser desorption and fast atom bombardment mass spectrometry of the GPI anchor before and after peracetylation. For the prodn. of monoclonal antibodies the purified GPI mol. was incorporated into liposomes and injected intrasplenically in BALB/c mice. After fusion with the myeloma cell line X63-Ag 8.653 hybridoma cells were cloned by single cell cloning. The secreted antibodies were characterized by ELISA, Ouchterlony immunodiffusion, and Western blot and used in first immunofluorescent studies.

L14 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:513461 CAPLUS
DOCUMENT NUMBER: 113:113461
TITLE: Production and characterization of antibodies against the cross-reacting determinant of glycosyl-phosphatidylinositol-anchored acetylcholinesterase
AUTHOR(S): Jaeger, Karin; Meyer, Pascale; Stieger, Susi; Brodbeck, Urs
CORPORATE SOURCE: Inst. Biochem. Molekularbiol., Univ. Bern, Bern, Switz.
SOURCE: Biochimica et Biophysica Acta (1990), 1039(3), 367-73
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dimeric acetylcholinesterase is anchored in the cell membrane by a glycosylphosphatidylinositol attached to the C-terminus of the protein. The complex glycan contains an antigenic epitope, the cross-reacting determinant (CRD), which is only revealed after removal of the diradylglycerol by phosphatidylinositol-specific phospholipase C (PI-PLC) but is cryptic in the amphiphilic form. Polyclonal antibodies were raised against the CRD of vertebrate acetylcholinesterase. The purified anti-CRD antibodies recognized only the PI-PLC treated hydrophilic forms of acetylcholinesterase. The purified anti-CRD antibodies recognized only the PI-PLC treated hydrophilic forms of acetylcholinesterase from bovine erythrocytes and Torpedo, and of variant surface glycoproteins from trypanosomes but not the corresponding amphiphilic proteins. Competition expts. showed that inositol-1,2-cyclic phosphate and glucosamine inhibited the binding of the antibodies to the CRD. Furthermore, binding of the anti-CRD antibodies to acetylcholinesterase contg. N-methylated glucosamine was markedly reduced. The amphiphilic N-methylated enzyme is less sensitive to digestion with PI-PLC than the nonmethylated form. Thus, inositol-1,2-cyclic phosphate and glucosamine, esp. the free amine group of this residue, contribute significantly to the epitope recognized by the anti-CRD antibodies.

L14 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 15
ACCESSION NUMBER: 1989:592936 CAPLUS
DOCUMENT NUMBER: 111:192936
TITLE: Antibodies to 5'-nucleotidase (CD73), a glycosylphosphatidylinositol-anchored protein, cause human peripheral blood T cells to proliferate
AUTHOR(S): Thompson, Linda F.; Ruedi, Julie M.; Glass, Alison; Low, Martin G.; Lucas, Alexander H.
CORPORATE SOURCE: Dep. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: J. Immunol. (1989), 143(6), 1815-21
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human peripheral blood T cells were stimulated to proliferate when cultured with submitogenic doses of PMA and goat antibodies to 5'-nucleotidase (5'-NT). The degree of proliferation, as measured by [³H]TdR incorporation on day 3, was similar to that achieved by stimulation with PHA. Anti-5'-NT antibodies had no effect on PHA-induced proliferation. Maximal stimulation was achieved with 0.6-1.0 ng/mL of PMA and 125 .mu.g/mL of IgG isolated from a goat anti-5'-NT antiserum. Both

intact IgG and F(ab')2 fragments were stimulatory. Interleukin 2 receptor expression and IL-2 secretion were also induced by anti-5'-NT antibodies and PMA. Anti-5'-NT-induced proliferation was inhibited >95% by a murine anti-IL-2 receptor mAb and required <0.3% monocytes. Similar results were obtained with a murine mAb specific for 5'-NT. As expected, anti-5'-NT antibodies and PMA did not induce the proliferation of ecto-5'-NT-T cells isolated by cell sorting. Pretreatment of total T cells with phosphatidylinositol-specific phospholipase C removed an av. of 89% of the 5'-NT activity from the cell surface and also inhibited by 83% the ability of the cells to proliferate in response to anti-5'-NT antibodies and PMA. Thus, the activation signal provided by anti-5'-NT antibodies is apparently transduced, in large part, by a form of the enzyme that is attached to the membrane via glycosyl-phosphatidylinositol linkage. The 5'-NT may play a role in lymphocyte activation as has been proposed for other glycosyl-phosphatidylinositol-anchored lymphocyte surface proteins.

L14 ANSWER 42 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1990:70518 BIOSIS

DOCUMENT NUMBER: BA89:38344

TITLE: MOLECULAR CHARACTERIZATION OF BABESIA-BOVIS MEROZOITE SURFACE PROTEINS BEARING EPITOPIES IMMUNODOMINANT IN PROTECTED CATTLE.

AUTHOR(S): HINES S A; MCWLWAIN T F; BUENING G M; PALMER G H DEP. VET. MICROBIOL. PATHOL., WASHINGTON STATE UNIV., PULLMAN, WASH. 99164-7030.

SOURCE: MOL BIOCHEM PARASITOL, (1989) 37 (1), 1-10.
CODEN: MBIPDP. ISSN: 0166-6851.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Eight surface-radioiodinated merozoite proteins from a cloned, pathogenic isolate of Babesia bovis can be immunoprecipitated by antibody from cattle that are completely against clinical babesiosis. Among these eight surface proteins, the 55- and 42-kDa molecules are biosynthetically labeled with [³H]glucosamine. The 42-kDa glycoprotein can also be labeled with [³H]myristic acid and partitions exclusively into the detergent phase in Triton X-114 extracts, indicating that it is an integral membrane protein and suggesting that it is anchored by a glycosylphosphatidylinositol** moiety. ***Antibody-mediated protection against B. bovis merozoites most probably requires a high level of circulating antibody to ensure antibody-merozoite binding during the parasite's brief extraerythrocytic phase. Antibodies in diluted sera selectively recognize the 120-, 85-, 55- and 42-kDa surface proteins. Only the 42-kDa integral membrane protein is reactive with serum antibodies diluted .gtoreq. 1:16 000. Thus, we hypothesize that these immunodominant proteins, especially the transmembrane 42-kDa glycoprotein, are important to the induction of the protective immune response and are candidates for an improved vaccine against babesiosis.

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002

L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
 L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
 L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
 L4 1 S L3 AND GPI-PLD
 L5 1504 S (IPG OR (INOSITOLPHOSPHOGLYCAN?))
 L6 4 S L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
 L7 3 DUP REM L6 (1 DUPLICATE REMOVED)
 L8 80 S L5 (1ON) ANTIBOD?
 L9 51 S L8 AND PD:19980327
 L10 25 DUP REM L9 (26 DUPLICATES REMOVED)
 L11 9525 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))
 L12 122 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) ANTIBOD?
 L13 67 S L12 AND PD:19980327
 L14 42 DUP REM L13 (25 DUPLICATES REMOVED)
 L15 0 S L14 (1ON) ADMINIST?
 L16 0 S L14 (P) ADMINIST?

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